



**ICH M2 EWG**

**Electronic Transmission of Individual Case Safety  
Reports Message Specification**  
**(ICH ICSR DTD Version 2.0)**

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This Specification has been developed by the ICH M2 Expert Working Group in accordance with the ICH Process as pertains to the M2 EWG.

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## **1.0 PURPOSE**

This document describes the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) M2 Document Type Definition (DTD) of the electronic message for the transmission of Individual Case Safety Reports (ICSRs) based on the ICH E2B step 4 document, Data Elements for Transmission of Individual Case Safety Reports.

The source of ICH official information is the ICH website: <http://www.ifpma.org/m2-main.html>.

## **2.0 BACKGROUND**

The ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission-European Union (EU), the European Federation of Pharmaceutical Industries' Associations (EFPIA), the Japan Ministry of Health and Welfare (MHW), the Japan Pharmaceutical Manufacturers Association (JPMA), the US Food and Drug Administration (FDA), and the Pharmaceutical Research and Manufacturers of America (PhRMA). The ICH Secretariat, which co-ordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization (WHO), the Canadian Health Protection Branch, and the European Free Trade Area.

To facilitate the standardization of the data elements for the transmission of ICSRs for both pre-approval and post-approval reporting periods, the ICH E2B Expert Working Group prepared the guideline "Data Elements for Transmission of Individual Case Safety Reports."

The guideline standardizes the data elements for the transmission of ICSRs by identifying and defining the data elements for the transmission of all types of ICSRs, regardless of source and destination. This includes case safety reports for both pre- and post-approval periods and covers both adverse drug reaction and adverse event (AE) reports.

The guideline states that because of national and international laws, rules, and regulations, ICSRs of adverse drug reactions and AE need to be transmitted:

- From identified reporting sources to regulatory authorities and pharmaceutical companies
- Between regulatory authorities
- Between pharmaceutical companies and regulatory authorities
- Within authorities or pharmaceutical companies

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- From clinical investigators, via the sponsor, to ethics committees
- From authorities to the WHO Collaborating Centre for International Drug Monitoring.

The transmission of ICSRs currently relies on paper-based formats (e.g., yellow cards, Council for International Organizations of Medical Sciences (CIOMS) forms, MedWatch) or electronic media (e.g., within pharmaceutical companies, or with WHO), usually via online access, tape, or file transfer.

Considering the high volume of data and the large number of potential participants in a world-wide exchange of information, there is a need for an electronic format capable of accommodating the electronic transmission of the Safety Reports that can be directly generated and processed by a database application.

Successful electronic transmission of ICSRs relies on the agreement of common data elements and on the syntactical definition of the electronic message.

The definition of the common data elements is provided in the E2B guideline. The syntactical definition of the electronic message is provided in the ICH M2 Expert Working Group (EWG) recommendations and specifications.

This document describes the specification of the message definition for the electronic transmission of ICSRs agreed by ICH M2.

## **2.1 Representation of the Electronic ICSR**

The ICH community agreed that the ICSRs, including pre-marketing and post-marketing adverse drug reactions and adverse drug events, should be gathered, managed, and distributed electronically, but there was a need to find consensus on how this should be done.

The objective was to represent the document in a way that would make possible transfer of its contents, from one database to another. In addition, the representation should use an international standard that is platform, application and vendor independent.

This initiative relied on the previous work done by the EuroScape consortium that had defined the MEDADR safety report in EDIFACT (Electronic Data Interchange for Administration, Commerce and Transport). There was also a large tradition of standardization of health related messages in HL7 (Health Level Seven), a specification used for electronic data exchange of healthcare information. As a result, both EDIFACT and HL7 syntax were originally considered for the formal specification of the electronic message for the transmission of safety reports of adverse drug reactions and adverse drug events. However, the need to support multi-lingual characters and the time it takes to get a new message approved for use by the standards organizations made Standard Generalized Markup Language (SGML, ISO 8879:1986) a better alternative.

SGML is an international standard for documents and it is also useful for the interchange of structured data. It presents some advantages:

- Validation of the message with available off-the-shelf software

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- Creation and processing of messages on current document technology.

In addition SGML document types facilitate the implementation of relevant functions:

- Interchange of data among different databases with heterogeneous data types
- Transformation of the data structure into relational databases
- Portability of data.

Information for electronic submission in SGML is prepared by inserting data appropriately between the start and end tags so the information maintains the relationships specified by the DTD. Typically, SGML editing tools can be used to prepare a data set that is specific to the SGML DTD.

In November 1996, in London, the ICH M2 EWG decided to concentrate the efforts to produce a DTD<sup>1</sup> of the message for the electronic transmission of ICSRs: the ICH\_ICSR.DTD.

At the following meeting of the ICH M2 EWG in March 1997 in Narita, the six parties agreed on the relational data model to be used for the definition of the electronic message based on the ICH E2B document Step 3 version 5.

Once the ICH E2B document was adopted as a Step 4 guideline in July 1997, the ICH M2 EWG finalised the relational model and the message definition, and the first official release of the ICH\_ICSR.DTD was agreed in October 1997 in Washington, DC. The official guidelines, recommendations and specifications for the ICH ICSR message definition can be obtained only from the ICH M2 website, <http://www.ifpma.org/m2-main.html>. Detailed instructions for preparing SGML data are also available from the manuals section of the website.

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<sup>1</sup> An SGML conformant document consists of an SGML prologue and a document instance. The prologue contains an SGML declaration and a document type definition, which contains element and entity declarations. Different software applications may provide different ways of associating the document instance with the prologue and in some cases the prologue may be inserted into the software used, so that it is transparent to the user.

The SGML declaration specifies basic facts about the dialect of SGML being used, such as the character set, the codes used for SGML delimiters, and the length of identifiers.

The document type definition specifies the DTD against which the document instance is to be validated. Like the SGML declaration, it may be held in the form of compiled tables within the SGML processor, or associated with it in some way that is invisible to the user, or require only that the name of the document type be specified before the document is validated.

The data instance is the content of the data itself. It may contain text, mark-up, and general entity references.

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As a result of this activity, AE data can be extracted, populated, and electronically transmitted in the manner specified by the ICH ICSR message from safety and surveillance databases.

## **3.0 ESSENTIAL COMPONENTS**

Developing software specifications to meet requirements, such as those specified in the E2B document, requires an approach where the functional and procedural requirements are well understood and reflected accurately in the electronic message. The electronic message must constitute not only the definition of the data elements, but also maintain the required relationships between the elements for efficient information exchange. The development of the relational diagrams, an attribute list, numeric codes, and the ICH ICSR SGML DTD is a result of efforts to define software specifications to facilitate electronic submissions of ICSRs. The ICH ICSR message allows for the preparation of AE data sets that can accurately maintain and represent the intended purpose of the E2B document. Section 3 of this ICSR specification document lists the essential components required to develop usable ICH ICSR messages.

### **3.1 ICSR Relational Diagrams**

The following ICSR relational diagrams illustrate the relationship between the various sections and data elements defined in the E2B document and the field attributes for the ICH ICSR message and DTD descriptors. A box in the relational view diagram represents the entire related section of the E2B document and all the data elements in the related block of the attribute list. For example, box A.1 in the diagram, Identification of the Case Safety Report, represents the complete A.1 section of the E2B document and the A.1 block of elements listed in the attribute list. To maintain the intent of the E2B specifications and to represent the various mandatory, optional, single, and repeatable sections or fields, the relationships between the boxes also vary from as much as a 1 to 1 relationship, a 1 to 0 or 1 relationship, a 1 to 1 or many relationship, or a 1 to 0 or many relationship. These diagrams are particularly useful for database administrators and application developers in understanding how the ICSR SGML DTD was designed and developed per the E2B specification document.

### 3.1.1 M2 Relational View of E2B Data Elements

The ICH M2 relational view of the E2B data elements shows the order and relationship between the various sections of the E2B document. This diagram (Figure 1) is useful in understanding how the various sections in the E2B document are organized and related to one another.

### M2 Relational View of E2B Data Elements

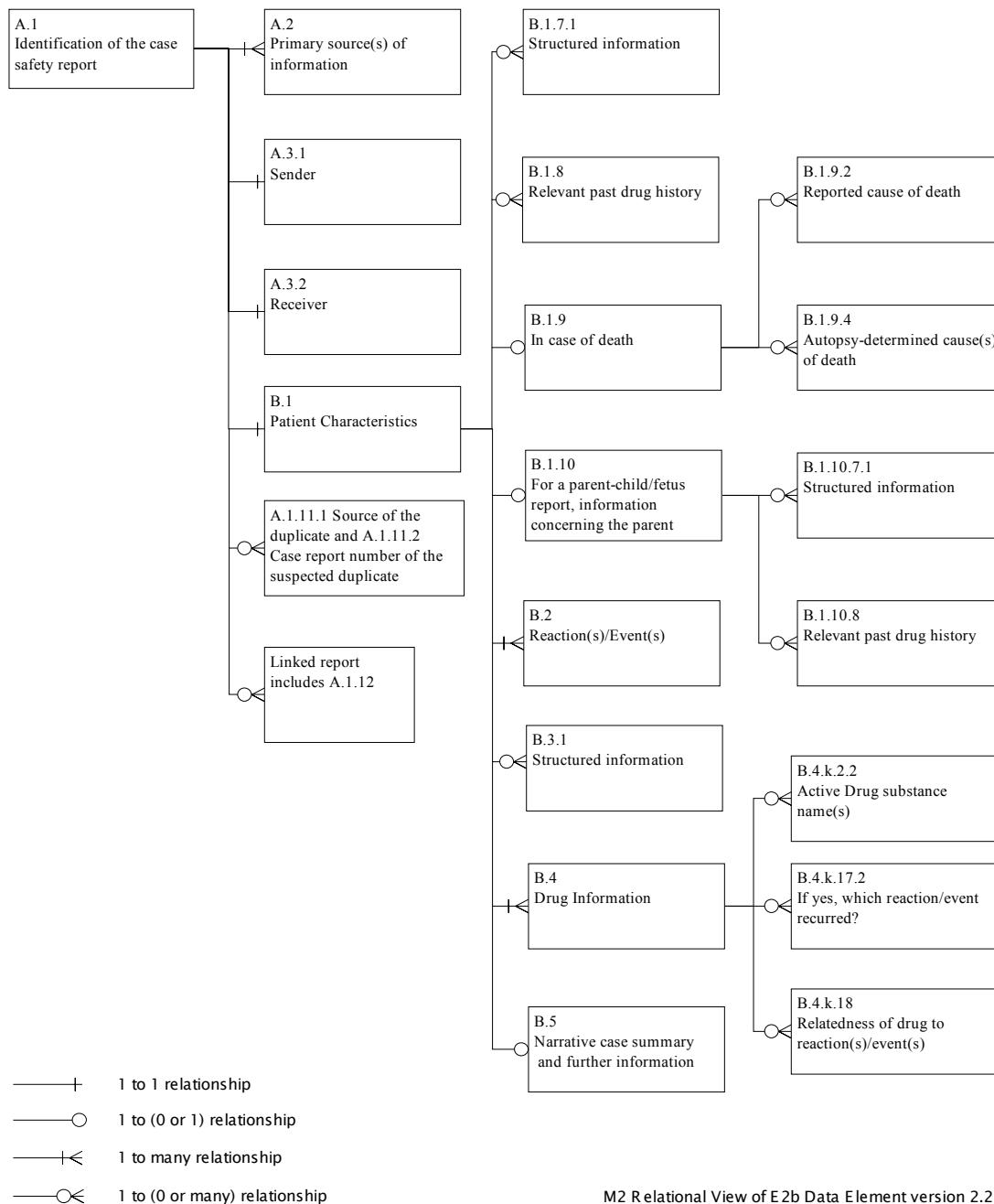


Figure 1

### 3.1.2 M2 Entities and Relationships Diagram

The M2 Entities and Relationships diagram (Figure 2) depicts the M2 defined entities and their relationships to the E2B data elements. The field names are found in the description column of the ICSR attributes list for the ICH ICSR message and DTD.

## M2 Entities and Relationships

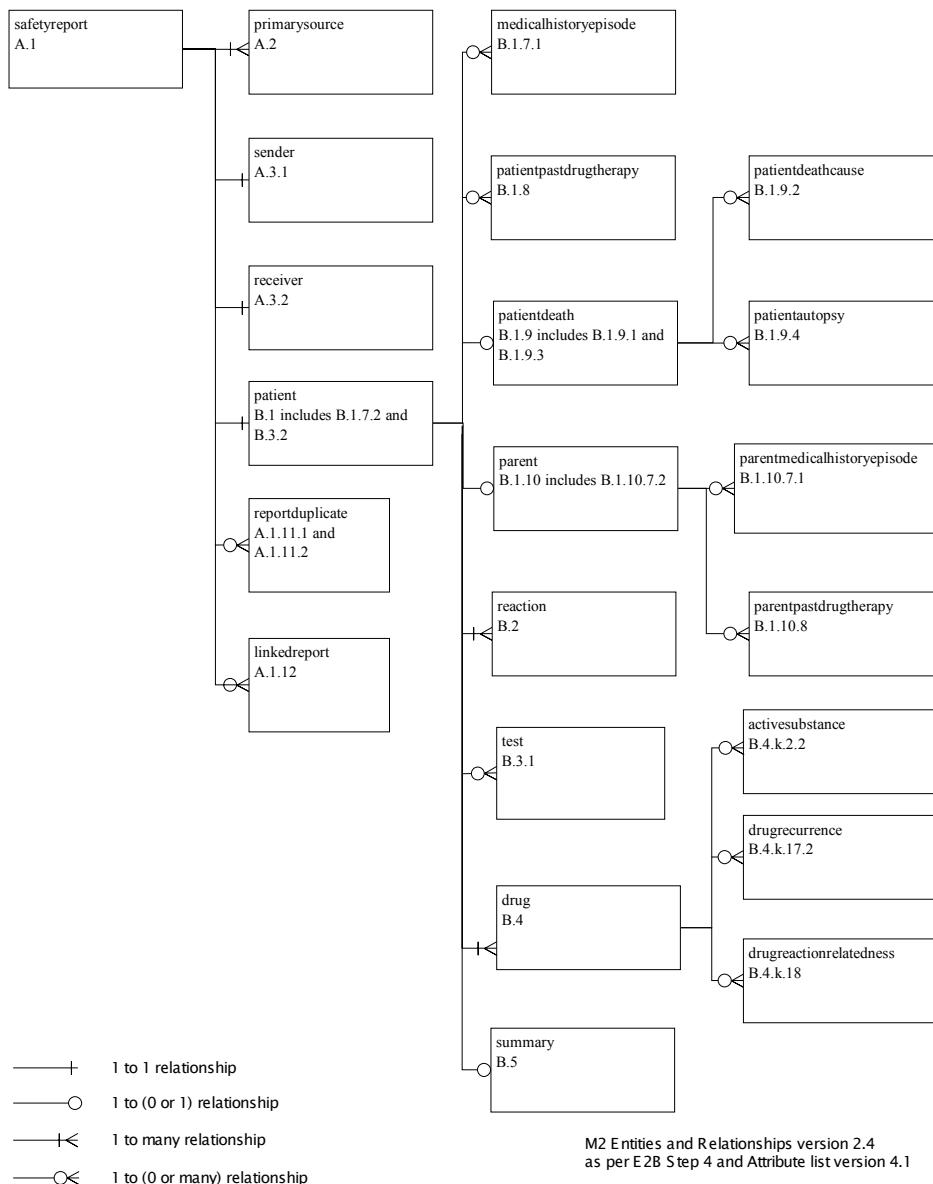


Figure 2

# **Electronic Transmission of Individual Case Safety Reports Message Specification**

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The entities and relationships diagram is similar to the relational view diagram, but it is particularly helpful to bridge the gap from the M2 relational view diagram to the ICSR attribute list, and eventually to the ICSR SGML DTD.

## **3.2 ICH ICSR Attribute List**

This ICSR specification document contains the ICH M2 attribute list with SGML descriptor names per the E2B document in Appendix A.1. This ICSR attribute list contains the data element number, title, description, field length, field value, and DTD descriptor for each data element. The various elements are also grouped and numbered to match with the organization of the E2B document. The attribute list has three types of blocks, depicted as a regular single line border, bold lined border, and double lined border. Fields within the single line border can occur once or not at all, while fields or blocks with a bold border might be repeated, and fields or blocks with a double line border might also be repeated, within the containing block. The ICH M2 field attribute list must be used to verify the accuracy and compliance of data entered when preparing an ICSR SGML data file.

To help manage, route, identify, and track ICH ICSR messages in the three ICH regions, and to help automate electronic submissions of ICSRs, the M2 group has also defined the following elements for a message header section. The detailed specifications of these elements are mentioned in Appendix A.1.

### **ICH ICSR Message Header**

This is a section header for the message header. This section assumes the establishment of an EDI trading partnership agreement that will help define the message number, sender ID, receiver ID, message date.

### **Message Type**

The message type contains information on the type of information being transmitted. It is specified in the M2 Recommendation 5.3. When creating an ICH ICSR message, the value of this field should be “ichicsr”.

### **Message Format Version**

The message format version contains the version number of the DTD and it is specified in M2 Recommendation 5.3. The value of the version number can be obtained from the documentation section of the ICH ICSR DTD.

### **Message Format Release**

The message format release contains the release number of the message format version number of the DTD and it is specified in M2 Recommendation 5.3. The value of the release number can be obtained from the documentation section of the ICH ICSR DTD.

### **Message Number, Sender defined message number (unique to the sender)**

The message number is a unique tracking number assigned to a specific ICH ICSR message file transmitted by the sender. This message number is unique to the sender.

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**Message Sender Identifier**

This field identifies the sender of the ICSR reports, e.g., company name or regulatory authority name (ICSR Attribute List A.3.1.2).

**Message Receiver Identifier**

This field identifies the intended recipient of the transmission of ICSR reports, e.g., company name or regulatory authority name (ICSR Attribute List A.3.2.2a).

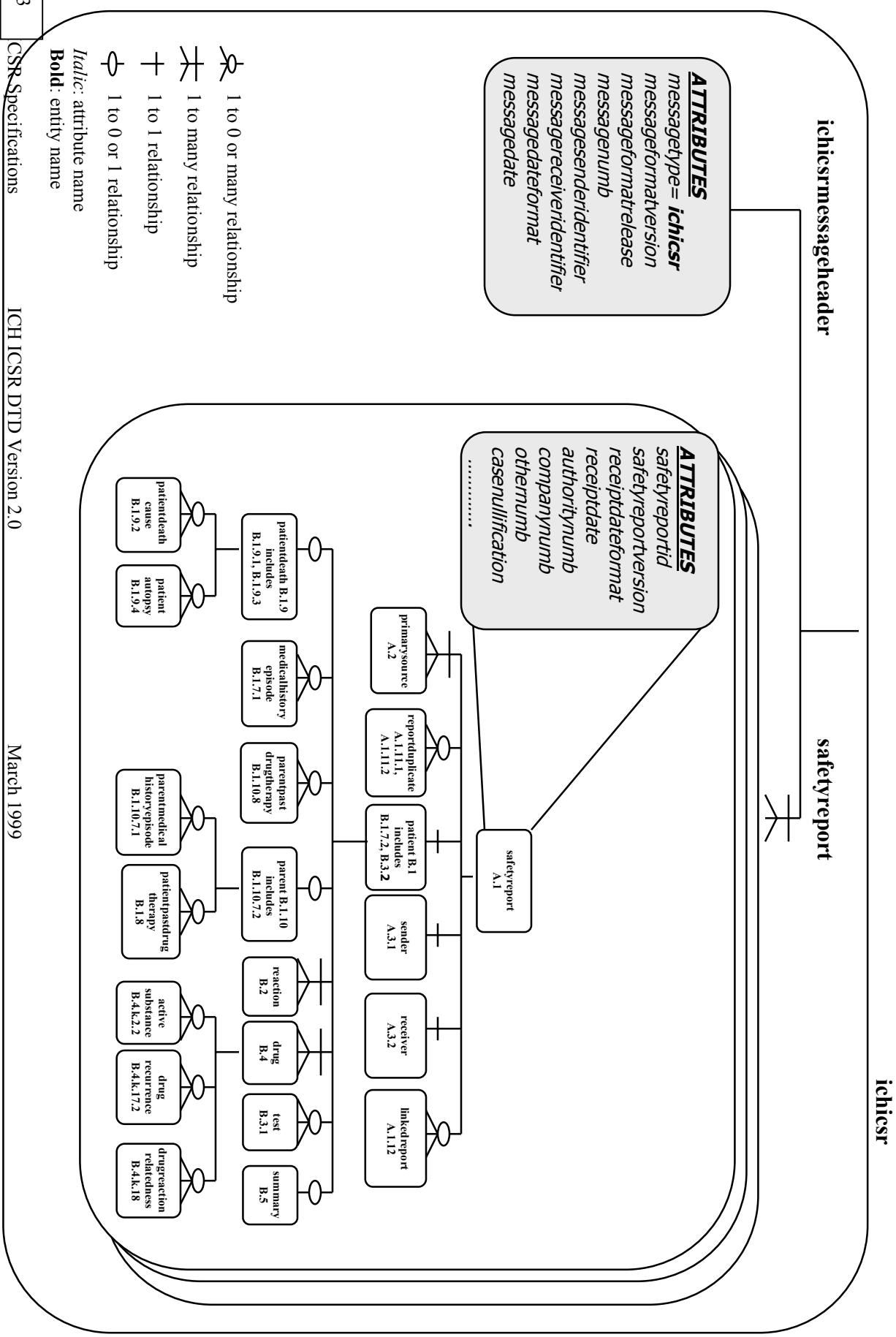
**Message Date and Format**

The message date is the date on which the ICH ICSR message was initiated.

The diagram on the next page illustrates the specified relationship where each ICH ICSR message will have one message header section, and one or more ICSRs.

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## ICH M2 Safety Message



### **3.3 ICH ICSR DTD**

The DTD describes each element of the ICSR being transmitted and shows how the various elements relate to each other. Within the encoded text, the DTD specifies which elements are required and the order in which they appear. According to the model specified in the DTD, each ICSR consists of one message header, followed by one or more ICSRs. Please refer to Appendix A.2 for a full text definition of this document. The original document can be obtained from the M2 website at the following URL: <http://www.ifpma.org/m2-main.html>.

To make improvements to version 1.0 of the ICH ICSR DTD, the M2 Expert Working Group has made the following modifications that are reflected in ICH ICSR DTD, Version 2.0. The documentation section of version 2.0 contains the complete list of changes.

- The ICH ICSR DTD, version 2.0 is now designed to support multiple language character sets to meet the diverse and complex reporting requirements of all the ICH regions. The details on the use of multiple language character sets are described in section 6.0 of this document.
- To help manage, route, identify, and track ICH ICSR messages, new elements have been added to the message header section of the ICH ICSR DTD.
- Data prepared for the ICH ICSR, version 1.0 required that no carriage returns be inserted after end tags. This was because version 1.0 of the ICH ICSR DTD was sensitive to carriage returns. Often, inserting carriage returns, after end tags caused SGML errors when the file was parsed. This was caused by the use of “mixed content models” within the DTD, and in particular with the way sequence numbers were represented. It is not necessary to understand the details of the SGML concept of a mixed content model, other than to point out that using it within the ICH ICSR DTD version 1.0 caused unpredictable parsing errors, when carriage returns were inserted after the end tags. This absence of carriage returns in turn made the SGML documents difficult to read.

To make the SGML data more readable, by permitting insertion of carriage returns after end tags and to eliminate the mixed content model problem, the sequence number elements (all XXXXsq elements) were removed. However, to maintain compliance with the relational model, the SGML specification had to be modified so that the higher level entities were specified as (+) for 1 or more or (\*) for 0 or more.

The following table illustrates how data is prepared without the use of sequence numbers. In version 1.0, repeating elements had a sequence number, such as <reportduplicatesq> for <reportduplicate>. The elements related to the sequence number, such as <duplicatesource> and <dupecatenumb> were repeated within a sequence. For version 2.0 of the ICH ICSR DTD, the data elements that required multiple occurrences are repeated, such as <duplicatesource> and <dupecatenumb> within <reportduplicate>.

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	<b>ICSR DTD</b>	<b>ICSR SGML Data</b>
<b>Specification for ICH ICSR, Version 1.0</b>	Medicallyconfirm? & (reportduplicate? & linkedreport? & .....  <!ELEMENT reportduplicate (reportduplicatesq*)> <!ELEMENT reportduplicatesq -- (#PCDATA, (duplicatesource? & duplicatenumb? ))> <!ATTLIST reportduplicatesq %ope.rec; >	<medicallyconfirm>1</medicallyconfirm> <reportduplicate><reportduplicatesq>001< duplicatesource> smith, coopers, barnies, and young pharmaceuticals </duplicatesource><duplicatenumb> nmbr1234567891011121314151617181920</ duplicatenumb></reportduplicatesq><report duplicatesq>002<duplicatesource> smith, coopers, barnies, and young pharmaceuticals </duplicatesource><duplicatenumb> number12345678910111213141516171819</ duplicatenumb></reportduplicatesq></reportd uplicate>
<b>Specification for ICH ICSR, Version 2.0</b>	Medicallyconfirm? , (reportduplicate* , linkedreport* , primarysource+ , .....  <!ELEMENT reportduplicate (duplicatesource?, duplicatenumb?)> <!ATTLIST reportduplicate %lang.att; >	<medicallyconfirm>1</medicallyconfirm> <reportduplicate> <duplicatesource>smith, coopers, barnies, and young pharmaceuticals</duplicatesource> <duplicatenumb>nmb12345678910111213 14151617181920</duplicatenumb> </reportduplicate>  <reportduplicate> <duplicatesource>smith, coopers, barnies, and young pharmaceuticals</duplicatesource> <duplicatenumb>number1234567891011121 3141516171819</duplicatenumb> </reportduplicate>

- The data elements in the ICH ICSR DTD version 1.0 could occur in any order. Now the specifications are tighter, requiring a specific order.
- APP/REP/DEL was removed in version 2.0 to ensure that each ICSR submission will contain as much information as is available at the time of submission (i.e., “complete submission”). The %act.rec; and %ope.rec; internal entities, were removed, thus removing all support for the "(app | rep | del )" construct. This also removes all support for "old" attribute.
- References to “old” attribute were removed from version 2.0 of the DTD to ensure that new or changed information will not be electronically “highlighted” on electronic ICSR submissions.
- The “lang” attribute was added to all the elements of the ICH ICSR DTD to ensure that data in multiple languages can be supported.
- To cover all of the languages necessary to support the use of the ICH ICSR message, five declaration (DCL) files, including one for ISO 10646 (UNICODE), are distributed with the DTD. Additional information on the DCL files is provided in section 3.4 of this document.

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- Special characters, such as "<" or "&", are represented according to the SGML standard. Specifications have been added to allow for standard character entities to escape SGML special characters. When "<", ">", and "&" occurred in text, they can be replaced by "&lt;", "&gt;", and "&amp;" respectively.
- The relationship between Drug and Active Substance was changed from a 1 to 1 or many relationship to a 1 to 0 or many relationship, in version 2.0 of the ICH ICSR DTD.
- The data model of the ICH ICSR message has been modified so that the root element of DTD is now "ichicsr" which is related to one "ichicsrmessageheader" and multiple (1 or more) "safetyreport" (See Figure 3).
- A tag, safetyreportversion, has been added to go with safetyreportid to meet the need for recording the version number of the safetyreportid. A sender of an ICH ICSR message might assign a number to the safetyreportid, to identify each ICSR, and assign a number to safetyreportversion to differentiate the different versions of an ICSR.
- The field resultstestsprocedures (E2B – B.3.2 Results of test and procedures relevant to the investigation of the patient) is now an optional field.
- The lengths of certain fields have been changed to meet the business requirements.

## **3.4 DCL Files for Multi-Language Character Sets**

The DCL (declaration) file describes the capabilities of an SGML system. It includes the following information: the character encoding used in the DTD and the document, the amount of system resources required by the DTD, the delimiters used in marking up the document, the SGML features used by the document markup, and other information specific to the application.

The SGML declaration provides several critical pieces of information to the SGML parser that allow it to correctly interpret an SGML document. Relevant to the use of the ICH ICSR message is the SGML declaration's function to tell the SGML parser which character set has been used to encode an SGML document. Because ICH ICSR messages may be interchanged in several languages, and because each language may require a different character set, the SGML declaration becomes critical in documenting which character set is being used in an ICH ICSR message.

SGML was designed with the assumption that only one character set would be used within any one document. As such, an SGML declaration documents a single character set, and expects that any one SGML document will be encoded with a single character set. A single character set may be able to represent more than one language. The ASCII character set can only represent English, however the ISO 8858-1 character set can represent most of the Western European languages, and ISO 10646 (UNICODE) can represent almost all of the worlds currently written languages.

To meet the multi-language capabilities of the three regions, five different DCL files have been provided for use with the ICH ICSR, version 2.0 and the ICSR Acknowledgment Message DTDs. The receiver of the SGML message needs to know which of the five DCL

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files were used for the reports. For example, one way might be to use the trading partnership agreement to specify the type of DCL file that can be used for the submission.

The DCL files along with brief descriptions of their purpose are provided in Appendix A.3. The ICH ICSR and ICSR Acknowledgment DTDs also have a technical note with instructions on appropriate use and brief descriptions of the five DCL files.

### **3.5 ICH M2 Numeric Codes for E2B Unit Codes and Routes of Administration**

E2B has specified various unit codes and routes of administration codes for population of certain fields. To facilitate efficient data transport, validation, and information exchange, the M2 EWG has provided numeric codes for both the unit codes and the routes of administration.

#### **3.5.1 ICH M2 Numeric Codes for Unit List (E2B Attachment 1)**

The ICH M2 numeric codes, listed in Appendix A.4, must be used to populate fields that require the E2B unit list, documented in Attachment 1 of the E2B document. The three digit ICH M2 numeric codes represent unit measurements for mass, volume, radioactivity, other units, and unit intervals.

#### **3.5.2 Routes of Administration (E2B Attachment 2)**

The three digit numeric codes provided in Appendix A.5 must be used to populate fields that require the E2B routes of administration, documented in Attachment 2 of the E2B document. The M2 numeric codes represent various pre-defined routes of administration. For example, the fields B.4.k.8 - drugadministrationroute and B.4.k.9 - drugparadministration require to be populated with the codes for the E2B routes of administration.

### **3.6 E2B Document on Data Elements for the Transmission of Individual Case Safety Reports**

The E2B document provides a detailed breakdown of the data elements for the ICSR, as well as notes on transmission and user guidance information. The E2B document provides the appropriate background, scope, and detailed specifications on the data elements for the transmission of all types of ICSRs. In order to comply with the standardized data elements for the successful electronic transmission of information, it is vital for the user to understand the E2B document. A copy of this document can be obtained from the ICH Web Site, hosted on the IFPMA server, URL: <http://www.ifpma.org/pdfifpma/e2b.pdf>.

## **4.0 APPROACH TO PREPARING ICSR SGML DATA FILES**

Extracting, translating, populating, and packaging adverse events (AE) data from heterogeneous AE databases can be complex. The M2 specifications, such as the relational view diagram, entity relationship diagram, attribute list, codes for E2B route of administration list and unit list, and the ICH ICSR DTD have to be used to develop an electronic ICSR that complies with the E2B document. This section is provided to help users understand the relationship between these products to develop valid electronic ICSRs that can be transported and loaded into receiving databases.

This section does not provide guidance on the interpretation of the E2B field specifications. The E2B document must be referenced and thoroughly understood to derive the intent of each field and the ICSR.

### **4.1 Organization Required for Preparing ICSR SGML Data Sets**

Using the ICH ICSR DTD to prepare electronic ICSRs requires an organized approach and an understanding of the content and intended use of the ICH E2B document and the various M2 products. As shown in Figure 4, the process should begin with an in-depth study of the E2B document, to understand the intent of the report and interpret the content and appropriate use of the data definitions. The E2B data elements should then be mapped to corresponding data elements in the AE databases, with the help of the M2 relational view diagram, entity relationship diagram, and attribute list. This is an important step and all measures must be taken to ensure that the correct data values are extracted from existing AE databases to populate the SGML data file. Once the AE data has been mapped to the ICSR schema, internal procedures and software routines must be used to extract, translate, populate, and prepare the SGML data file. The figure below shows the process for the electronic submission of ICSRs.

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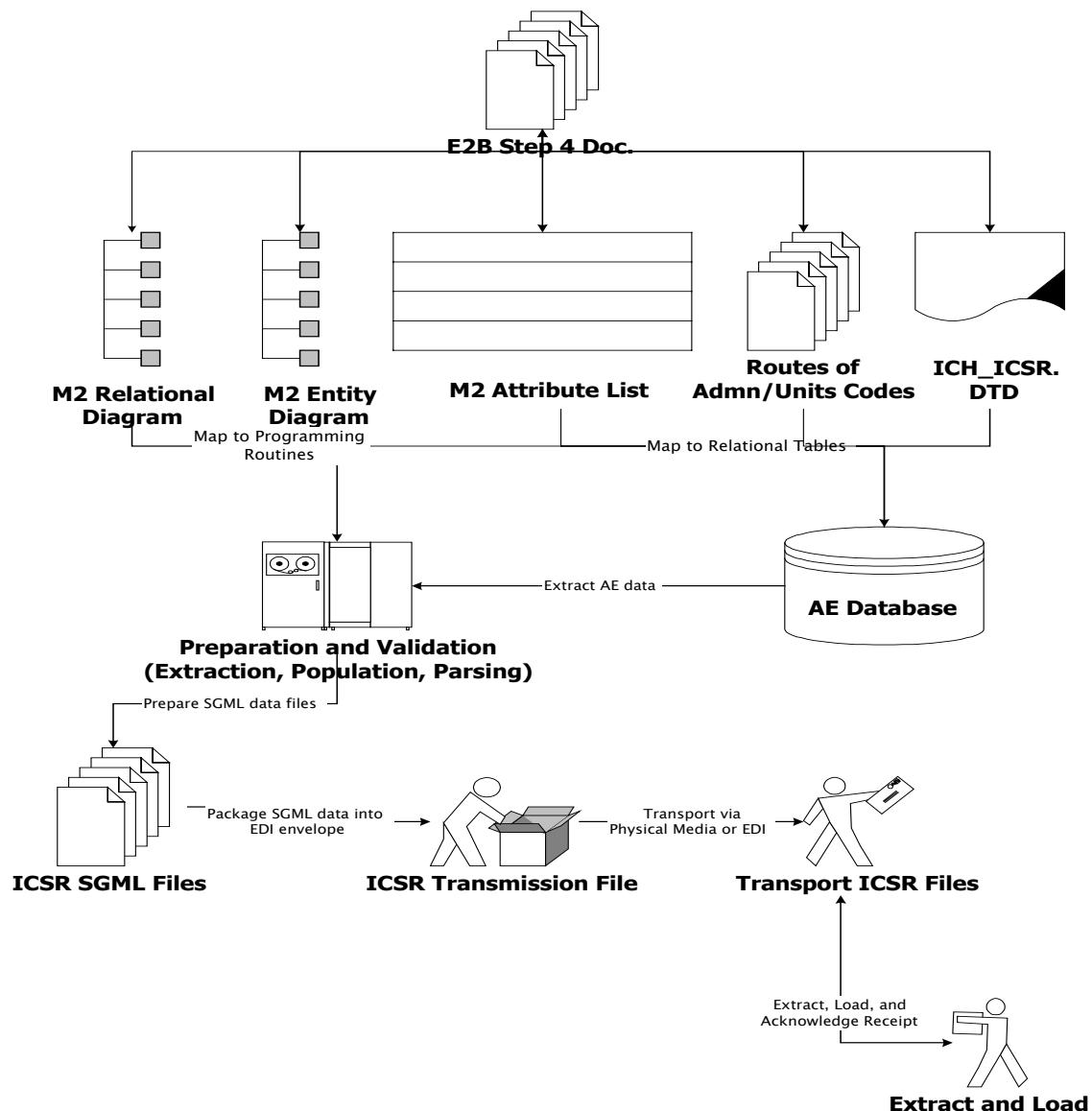


Figure 4

The following section provides step-by-step instructions for creating an SGML data file. Please refer to the ICH M2 website for additional information: <http://www.ifpma.org/m2-main.html>.

#### 4.2 Step-By-Step Instructions on How to Prepare a Data File

This section explains some basic steps to help prepare a SGML data set that is compliant with the ICH ICSR DTD and can be used for the electronic transmission of structured individual case safety data.

The E2B document, the M2 relational view diagram, the ICSR attribute list, and the DTD descriptors must be used as a reference while entering data to verify the accuracy of the DTD descriptor and E2B field definitions. AE data must be extracted from safety and surveillance

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databases in a manner specified by the ICH ICSR message. Information for electronic submission is prepared by inserting data appropriately between the start and end tags so the information maintains the relationships specified by the DTD. Typically, SGML editing tools can be used to prepare a data set that is specific to an SGML DTD. The SGML tools check for valid SGML rules and provide efficient features, like automatic insertion of start and end tags to make the task of preparing data easier. However, in the absence of SGML editing tools, a word processor or simple text editor can also be used in the following manner:

- Open ICH\_ICSR.DTD.
- Define the appropriate tags for each DTD element.

For example, in the new document, define tag as <ichicsr> for element defined in DTD as <!ELEMENT ichicsr - - (ichicsrmessageheader, safetyreport+)>.

- AE data must be placed after the open tag of the appropriate descriptors defined in the new text file. To verify that data are populated appropriately, check the E2B document and M2 field attribute spreadsheet (Appendix A.1) for field definitions, titles, field lengths, field values, and descriptor names.

For example, in the populated SGML file – ich-icsr-v2.0-19981018-test-english.sgm, the value “US” is entered after the field descriptor <primarysourcecountry>, as <primarysourcecountry>US. This value was entered after verifying that the tag <primarysourcecountry> referred to the E2B field A 1.1, identification of the country where the reaction/event, with DTD descriptor <primarysourcecountry>, field length of 2AN, and a country code compliant with ISO3166, US.

- Make sure that there is an end tag for every start tag.

For example, <tagname> must be followed by </tagname>  
<primarysourcecountry>US</primarysourcecountry>

- Between the start and end tag of a large text field, such as 200AN or longer, you can have carriage returns to make the data more readable.

For example,  
<>nullificationreason>invalid information regarding...  
.....  
the drug reaction  
</nullificationreason>

- The repeatable fields and sections (designated by a double line box in the M2 field attribute list) are populated by copying and pasting the DTD descriptors as necessary, then populating them with data.

Note: Each section that is repeated, must begin with the section name (e.g. <reportduplicate> and end with the corresponding end tag (back slash before the same title (e.g. </reportduplicate>)).

For example:  
<reportduplicate>  
<duplicatesource>smith, coopers, barnies, and young  
pharmaceuticals</duplicatesource>

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```
<dupe>nmb1234567891011121314151617181920</dupe>
</reportduplicate>
<reportduplicate>
<dupe>smith, coopers, barnies, and young
pharmaceuticals</dupe>
<dupe>number12345678910111213141516171819</dupe>
</reportduplicate>
<linkedreport>
<linkreportnumb>12345678910111213141516171819202122</linkreportnumb>
</linkedreport>
<linkedreport>
<linkreportnumb>report number 123456789101234567891</linkreportnumb>
</linkedreport>
```

- However, if there is no data for an optional block, then the complete block must be omitted. For example, since reportduplicate is an optional block and if there is no report duplicate information, then the complete block shown above, beginning with <reportduplicate> and ending with the </reportduplicate> must be omitted.
- For further illustration, the following scripts are provided as an example of a DTD definition and the corresponding syntax of a populated SGML file. Appendices A.2 and A.7 provide the definitions of the ICH ICSR and ICSR Acknowledgment DTDs. Appendix A.8 provides the definition of a sample ICSR Acknowledgment SGML data file.

Part of the ICH\_ICSR.DTD:

```
<!ELEMENT safetyreport      - ->
  (safetyreportid?,
   safetyreportversion?,
   primarysourcecountry?
   occurcountry?
   transmissiondateformat?
   transmissiondate?
   reporttype?
   serious?
   seriousnessdeath?
   seriousnesslifethreatening?
   seriousnesshospitalization?
   seriousnessdisabling?
   seriousnesscongenitalanomaly?
   seriousnessother?
   receivedateformat?
   receivedate?
   receiptdateformat?
   receiptdate?
   additionaldocument?)
```

Sample SGML data file:

```
<safetyreport>
  <safetyreportid>0001</safetyreportid>
  <safetyreportversion>1.0</safetyreportversion>
  <primarysourcecountry>US</primarysourcecountry>
  <occurcountry>US</occurcountry>
  <transmissiondateformat>102</transmissiondateformat>
  <transmissiondate>19980101</transmissiondate>
  <reporttype>1</reporttype>
```

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```
<serious>1</serious>
<seriousnessdeath>1</seriousnessdeath>
<seriousnesslifethreatening>1</seriousnesslifethreatening>
<seriousnesshospitalization>1</seriousnesshospitalization>
<seriousnessdisabling>2</seriousnessdisabling>
<seriousnesscongenitalanomaly>2</seriousnesscongenitalanomaly>
<seriousnessother>2</seriousnessother>
<receivedateformat>102</receivedateformat>
<receivevatedate>19980102</receivevatedate>
<receiptdateformat>102</receiptdateformat>
<receiptdate>19970103</receiptdate>
<additionaldocument>1</additionaldocument>
```

Once all the E2B compliant information is entered in the appropriate sections, the document must be saved as, "filename.SGM". The SGML data file must then be parsed by an SGML parser, such as the James Clark SP parser, with reference to the ICH ICSR DTD, to ensure the file is syntactically error free. To parse the data file by using the James Clark SP parser, assuming that all of the files (DCL, DTD, and SGML) are in the same directory, the following command may be executed:

```
nsgmls -s declaration-file.dcl dtd-file.dtd sgml-file.sgm.
```

The "-s" is a flag that suppresses the normal output of "nsgmls". Only errors in the SGML files will be reported with the "-s" flag set and there shouldn't be any. The SGML data can be transmitted via physical media, such as CD-ROM, or via secure EDI. In the case of transmitting data via secure EDI over the Internet, the SGML data generally must be packaged by inserting it into an EDI envelope to facilitate the data transmission. The details of packaging data for EDI transmissions can be obtained from other sources, such as user manuals for EDI application software.

## 4.3 The Information Requirements for the Tracking and Routing of ICSRs

Multiple ICSRs can be sent in a single transmission, via physical media or secure EDI over the Internet. It is also important to correctly populate specific data elements to provide a link that will help uniquely identify an ICSR and the transmission message that contains the single or multiple ICSRs. To accomplish this unique identification of each ICSRs, it will be useful to adopt the following approach:

- For each electronic transmission of an ICH ICSR message, the following information must be provided in the M2 message header section, when submitting via physical media or via secure EDI over the Internet.

**Message Number, sender defined transmission number** – specify a transmission number that is unique to the sender. This number can also be incremental.

**Message Sender Identifier** – specify the identification of the sender of the ICSR message, e.g., company name or regulatory authority name (ICSR Attribute List A.3.1.2).

**Message Receiver Identifier** – specify the identification of the receiver of the ICSR message, e.g., company name or regulatory authority name (ICSR Attribute List A.3.2.2a).

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**Message Date** – specify the date and time on which the transmission of the message was initiated in the format CCYYMMDDHHMMSS.

- For each ICSR, the following information must be provided: Section 1.5 Minimum information of the E2B guideline must also be referenced.

**ICSR Identification Number** - A.1.10.2 Company's case report number, or A.1.10.1 National regulatory authority's case report number, or A.1.10.3 Other sender's case report number.

**Information Date** – A.1.7 Date of receipt of the most recent information.

**Identifier of Sender** - A.3.1.2 Sender identifier, e.g., company name or regulatory authority name.

If a sender suspects or knows that the report has already been transmitted to the receiver, the following information must be provided:

**Duplicate report** - A.1.11 Suspected duplicate (A.1.11.1 Source(s) of the duplicate, e.g., name of the company, name of regulatory agency and A.1.11.2 Case report number of the suspected duplicates).

Companies should ensure a single international report number to facilitate the unique identification of a report that may have been sent to many places and subject to multiple retransmissions. The contents of the A.1.10 fields (A.1.10.1, A.1.10.2, or A.1.10.3) should be populated only once and should remain unchanged for any transmissions subsequent to the original transmission. The value for these fields must be a concatenation of “country code-company name-report number” and should first list A.1.1 - Identification of the country of primary source and secondly list A.3.1.2 - Sender identifier, sender organization, and lastly, the company international case report number, delimited by hyphens.

For example, a report transmitted by a US company to a regulatory authority would populate A.1.10.2 with “US-Company Name-12345”, where “12345” is the company’s unique case report number. In the event that the regulatory authority transmitted this ICSR to another regulatory authority, A.1.10.2 would remain the same. The regulatory authority would not populate A.1.10.1.

Furthermore, in order to maintain the original value of A.1.10 for subsequent transmissions, a recipient of an ICSR can forward the same report to other organizations by populating the A.1.11 – Suspected duplicate fields, as illustrated in figure 5. In this example, company-A in the U.S. sends out a report to company-B in Japan and company-C in France, which is subsequently sent to company-D in Japan and company-E in the U.K. Each company also submits the report to a regulatory authority.

Company A’s case report number in A.1.10.2 will remain unchanged as each forwarding company enters its own case report number in A.1.11.2 – Case report number of the suspected duplicate field. Each company should also populate A.1.11 per the ICSR data model, where A.1.11 - Suspected duplicate has two related repeatable fields, A.1.11.1 - Source of the duplicate and A.1.11.2 - Case report number of the suspected duplicate. In this case, a forwarding company, such as company B, must populate A.1.11 with “1” for yes and place the name of the organization (Company B) in A.1.11.1 and its own unique

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identification number (JP-Company B-Rep001) in A.1.11.2. Subsequently, other forwarding companies, such as D and E will also fill their case report numbers in the repeatable A.1.11.2 field.

## Model of a Sample ICSR Transmission

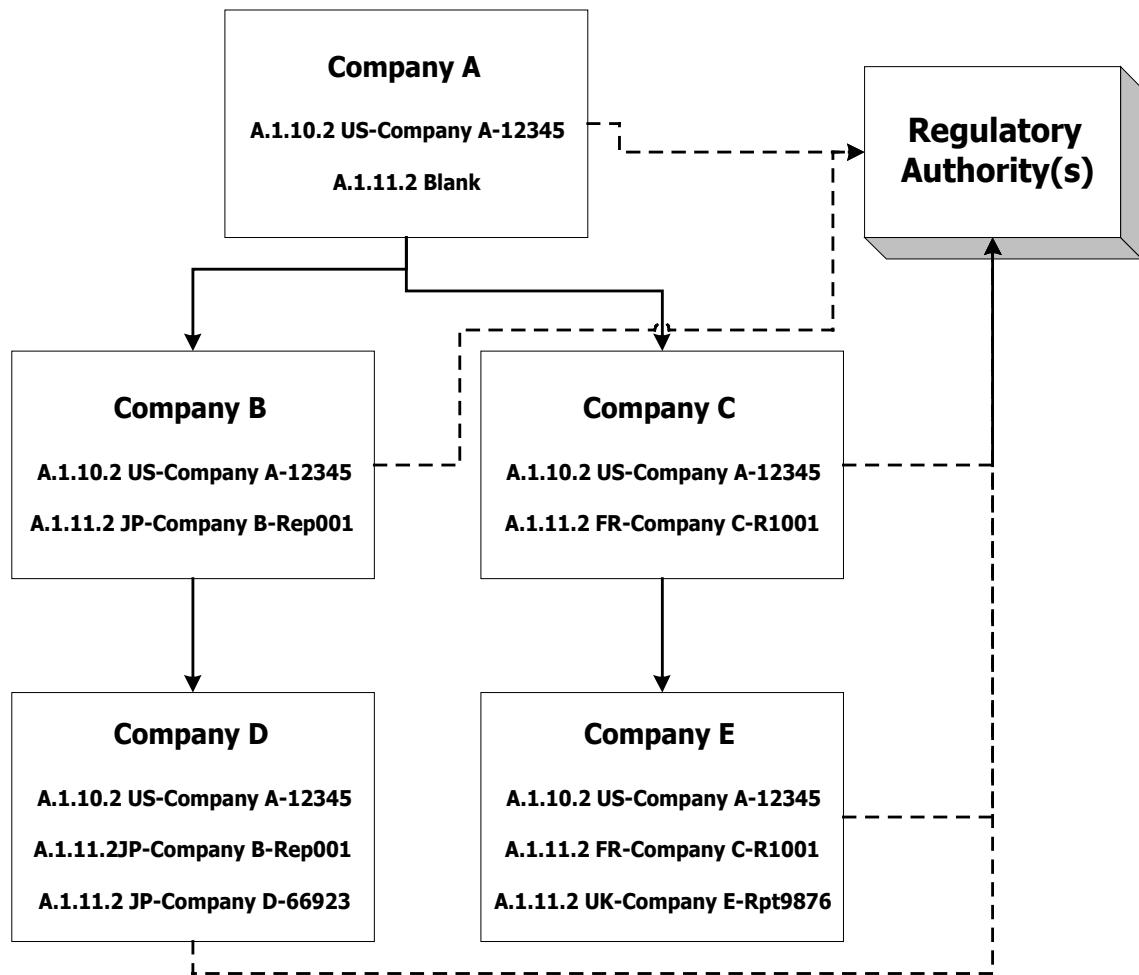


Figure 5

## **5.0 THE ICSR ACKNOWLEDGMENT MESSAGE**

The ICH M2 group has realized that to facilitate electronic submissions of ICSRs and to help pharmaceutical companies send useable data in a timely fashion, there is a need to provide feedback in an appropriate manner. The required feedback acknowledges receipt of the transmitted message as well as validating that each ICSR is syntactically correct and that data for all mandatory fields are provided.

To provide the required feedback for the ICH ICSR message, M2 has developed a specification for an ICSR Acknowledgment Message and corresponding SGML DTD, with appropriate validation and acknowledgment procedures, to support the requirements. The overall objective of developing an ICSR Acknowledgment Message is to help automate the status tracking of the electronic submission of ICSRs.

The following sections provide descriptions of the ICSR Acknowledgment Message. The data element specifications and message structure are contained in Appendix A.6. The ICSR Acknowledgment DTD is contained in Appendix A.7.

Typically a receiver of ICH ICSR messages will validate the incoming messages as described in the section below and create an SGML message to comply with the ICSR Acknowledgment DTD, specified in Appendix A.7. The details for creating the SGML message will be similar to the steps described in section 4.2. The sender of the ICSR message can then extract the data from this ICSR Acknowledgment Message, to determine the status of each ICSR.

### **5.1 Validation and Automated Acknowledgments of EDI Submissions**

The ICSR Acknowledgment allows receivers of the SGML data, such as regulatory authorities, to provide valuable feedback about the usability of the data in the transmission message. The ICSR Acknowledgment allows senders, typically pharmaceutical companies, to track and correct SGML syntax errors prior to re-transmission.

#### **Transmission file validation**

Once an EDI gateway decrypts and passes the file to the AE databases, an application parses the SGML data file to extract the structured information. If there is an SGML parsing error, the whole file is rejected and no further processing occurs. The sender must then re-transmit the same data file, after correcting the SGML file for syntactical or structural errors. The application software may be able to provide information about parsing errors and the acknowledgment message is used to convey information on such errors.

#### **ICSR Database Load Validation**

Once the data has been parsed without any errors from the SGML file, each report is loaded into the target AE database system. As each report is loaded into the data tables, each field is validated for:

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- Data type
- Data length
- Field value
- Required data.

The AE application will perform limited validations and will reject reports that don't have the required database fields. The system reports the status of each report as "loadable" or "not loadable" and requests re-transmission of only those reports that are not loadable into the database.

Once the reports are loaded into the application database, it becomes the responsibility of the regulatory authority to assess the reports.

## **5.2 Acknowledgment Message Format**

According to the model specified for the acknowledgment DTD, the ICSR Acknowledgment Message is comprised of two sections, each occurring once; the message header section and the acknowledgment section. The acknowledgment section is comprised of two portions, a message acknowledgment portion which occurs once, and a report acknowledgment portion which can occur one time, many times, or not at all.

### **Message Acknowledgment**

This section of the DTD specifies the required elements to indicate whether or not the SGML parser was able to extract the transmitted data. To help in tracking and identifying the transmission, this section includes the sender defined ICH ICSR message number, identifier of sender of the ICH ICSR message, identifier of receiver of the ICH ICSR message, message date, and a transmission acknowledgment code. The transmission acknowledgment code notifies the sender that one of the following is true:

- Parsing was successful and all ICSRs could be loaded into the target database
- Parsing was successful but not all ICSRs could be loaded into the target database
- The SGML file failed validation by an SGML parser.

The details of this specification are documented in Appendix A.7 of this document.

### **ICSR Report Acknowledgment**

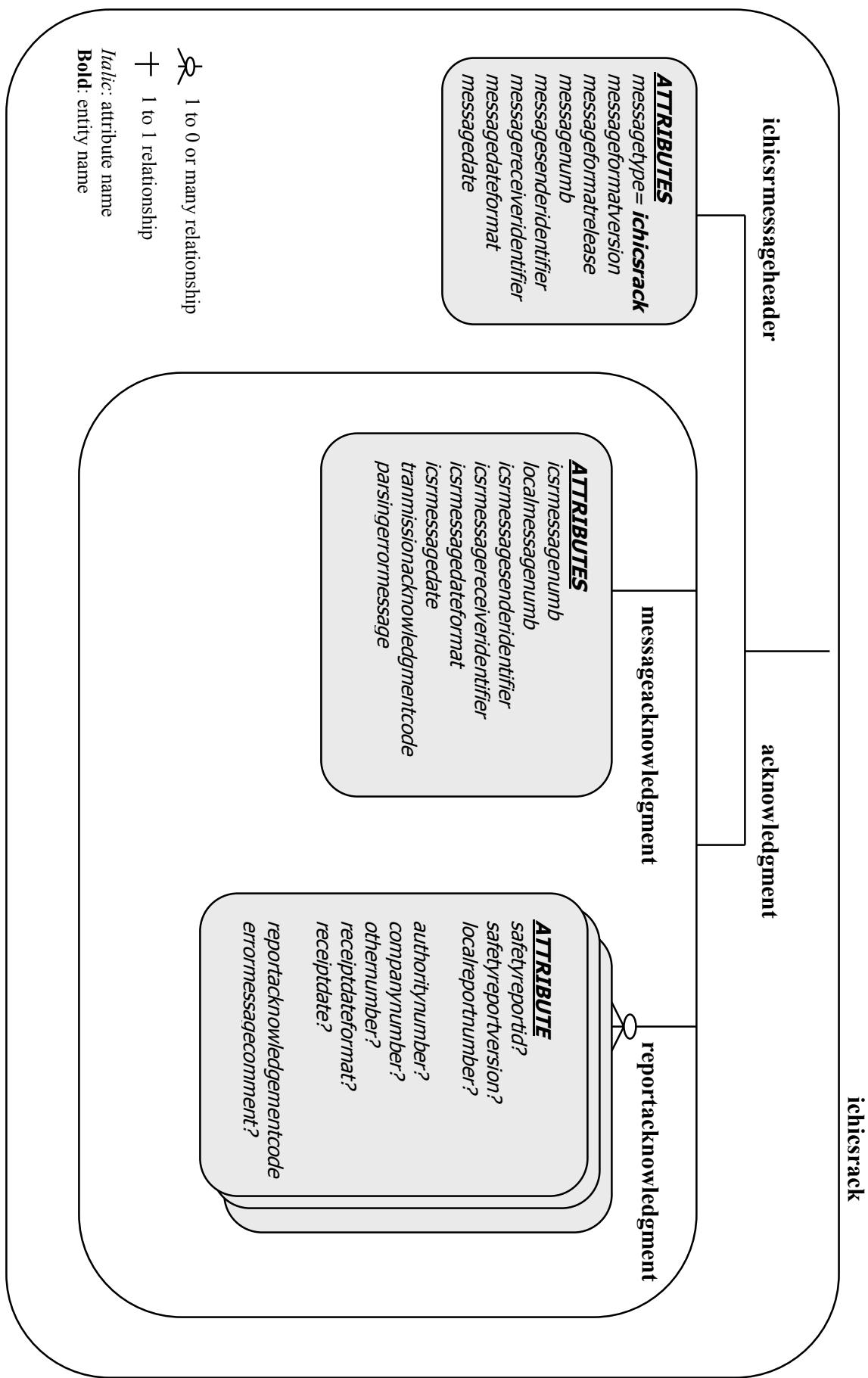
The ICSR report acknowledgment is a repeatable section for acknowledging each report included in the SGML file. This section provides information to help identify each ICSR, such as the safety report id, safety report version number local report number, company's case report number, and date of receipt of the most recent information. This section will also provide information on the errors encountered while loading the data into the relevant tables. This information will be particularly helpful for companies to improve the quality of the data,

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prior to re-transmission. The details of this specification are also documented in Appendix A.7 of this document.

The diagram on the next page illustrates the specified relationship, where each ICSR acknowledgment message includes the message header section, one message acknowledgment section and multiple acknowledgments for each safety report.

## ICH M2 Acknowledgment Message



## **6.0 MULTILINGUAL SUPPORT IN ICH ICSR MESSAGES**

There are two important features in version 2.0 that allow the development of an SGML data set that contains multi-language characters in a single SGML file. The first feature is that five different DCL files are distributed along with the ICH ICSR DTD, version 2.0. Correctly parsing an ICH ICSR message requires the selection of the correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance. Depending upon the character sets being transmitted, a reference should be made to a specific DCL file. The specifics on the DCL files with brief descriptions of their purpose are provided in Appendix A.3. The ICH ICSR and the ICSR Acknowledgment DTDs also have a technical note with instructions on appropriate use of the five DCL files.

The second feature is to know how to label the language being used in each field of an ICH ICSR message. This section describes the method to be used.

To accommodate the incorporation of multiple languages and to identify the various languages of the text within the various tags of an ICH ICSR message, a method of labeling the tags with a language attribute is used. This method is a common requirement in SGML applications and is a widely accepted technique for Hypertext Markup Language (HTML), SGML, and eXtensible Markup Language (XML). The method involves four rules:

- Rule 1: When an SGML element contains only character data, (as opposed to other SGML elements), that character data can only be in one language.
- Rule 2: An SGML attribute may be added to any SGML element to indicate the language of that element's content. This attribute is called "lang", and its value is one of the ISO 639 language digraphs. These digraphs are always entered in lower case.
- Rule 3: If a "lang" attribute is not set then the content of the element is assumed to be in the same language as the nearest containing element that does have a language attribute.
- Rule 4: The root element of the document is required to have a language attribute.

### **6.1 Directions on How to Use DTD to Support Multi-Language Characters**

To understand how these rules apply, it is first necessary to review a basic principle of SGML, namely that in SGML, documents consist of a collection of tagged elements that are nested within each other to form a hierarchy or tree. In the ICH ICSR message format the first, or root element of the tree is indicated in SGML by the tag <ichicsr>. The tag </ichicsr> indicates the end of the root element, and the end of the ICH ICSR message. Inside of these two tags all other ICH ICSR elements occur, each indicated by a tag that contains other tags, actual data, or a combination of the two. Graphically, a portion of the ICH ICSR document tree would look like Figure 7. In actuality, it would be represented in SGML as shown in Example 1, where indentation is used to highlight the nesting hierarchical structure of the SGML document.

### ICH ICSR Document Tree

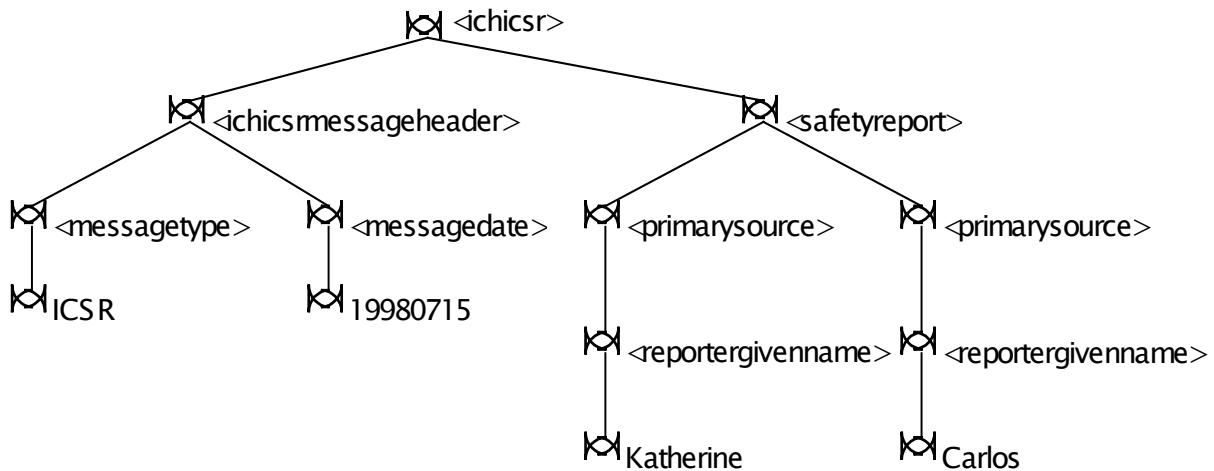


Figure 7

### Sample SGML Data Set

```

<ichicsr>
  <ichicsrmessageheader>
    <messagetype>ICSR</messagetype>
    <messagedate>19980715</messagedate>
  ...
  </ichicsrmessageheader>
  <safetyreport>
    <primarysource>
      <reportergivenname>Katherine</reportergivenname>
    </primarysource>
    <primarysource>
      <reportergivenname>Carlos</reportergivenname>
    </primarysource>
  </safetyreport>
</ichicsr>
  
```

Example 1

A new SGML message will now be constructed following the four rules outlined above. First, rule four states that the root element of the SGML document must have a lang attribute. For example, if the document will contain English, this would be indicated with the SGML attribute "lang" being set to the value "en" on the root element <ichicsr>, as illustrated in Example 2. Because of rule three, if no other language attributes are set on any element, all document content is assumed to be in English, because <ichicsr> "contains" all other elements in the document tree.

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Now assume that all of the information under <ichicsrmessageheader> should be in French. This would be accomplished by adding the attribute lang="fr" to the <ichicsrmessageheader> element. Now, all SGML elements subordinate to <ichicsrmessageheader> would be assumed to contain French. Finally look at <reportergivenname>Katherine</reportergivenname>. Indicate that this should be in Spanish by adding the now familiar lang attribute. It is important to note that <reportergivenname>Carlos</reportergivenname> is still assumed to be in English because its ancestor in the tree with a lang attribute is the root element <ichicsr>. The complete example is given in below, both in the graphical representation, and SGML syntax.

### ICH ICSR Document Tree Using the Language Attribute

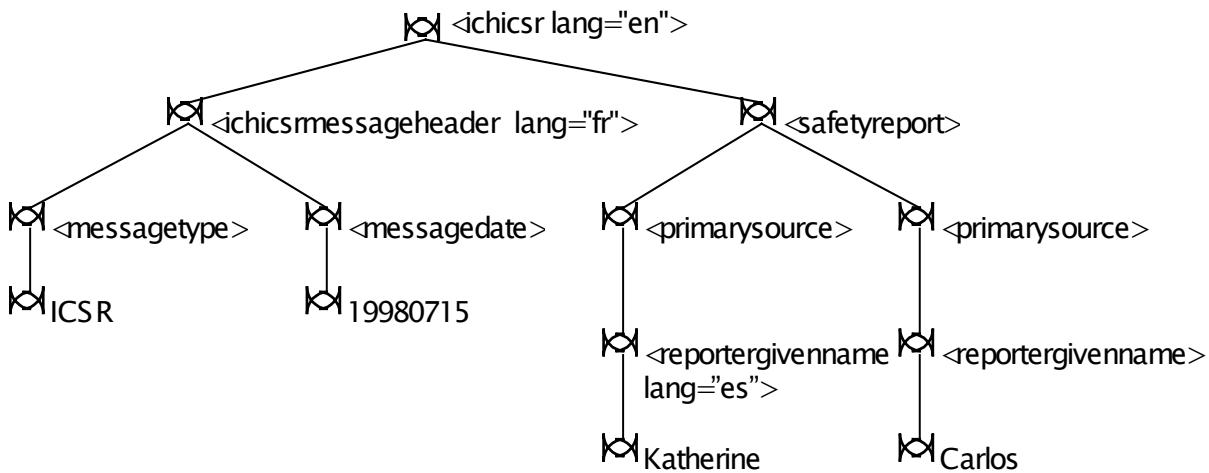


Figure 8

### Sample SGML Data Set Using the Language Attribute

```
<ichicsr lang="en">
  <ichicsrmessageheader lang="fr">
    <messagetype>ICSR</messagetype>
    <messagedate>19980715</messagedate>
...
  </ichicsrmessageheader>
  <safetyreport>
    <primarysource>
      <reportergivenname lang="es">Katherine</reportergivenname>
    </primarysource>
    <primarysource>
      <reportergivenname>Carlos</reportergivenname>
    </primarysource>
  </safetyreport>
</ichicsr>
```

Example 2

In summary, by following the four rules outlined in this section, multiple languages can be supported

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by the ICH ICSR message formats, with minimal impact on the complexity or size of the messages. **If the entire, ICH ICSR message is only in one language, then placing the “lang” attribute on the very first SGML tag <ichicsr> in the document is all that is required.** Moreover, because of the hierarchical structure of the SGML document itself, and the fact that a given use of the “lang” attribute effects all elements subordinate to it, the use of the “lang” attributes can be minimized. It is incumbent on applications that process this data know what language can be expected in each element. This can be accomplished by implementing a simple stack data structure to keep track of language information.

## A.0 APPENDIX

The following appendices contain specifications of the various components that have been referenced throughout the Electronic Transmission of ICSRs Message Specification document. These appendices provide the necessary details required to aid in the preparation of a valid ICH ICSR message, as well as ICSR Acknowledgment Message, for electronic submission. The appropriate appendices should be referenced along with the instructions provided in the specification document to understand the data requirements and the process for preparing a usable SGML message. The ICH M2 website (<http://www.ifpma.org/m2-main.html>) is the only source for obtaining the ICH ICSR DTD, ICSR Acknowledgment DTD, and the SGML DCL files for multi-language support.

The following references are for those preparing and sending ICH ICSRs:

- **Appendix A.1 - ICSR Attribute List**, used to verify the title, description, field length, field value, and DTD descriptor for each data element. The various elements are also grouped and numbered to match the organization of the E2B document. The attribute list has three types of blocks, depicted as a regular single line border, bold lined border, and double lined border. Fields within the single line border can occur once or not at all, while fields or blocks with a bold border might be repeated, and fields or blocks with a double line border might also be repeated, within the containing block. This attribute list must be used to verify the accuracy and compliance of data entered when preparing an ICSR SGML data file.
- **Appendix A.2 - ICH ICSR DTD**, used to describe the elements of the ICSR being transmitted. The DTD describes each element of the ICSR being transmitted and shows how the various elements relate to each other. Within the encoded text, the DTD specifies which elements are required and where they may appear, as well as their order of appearance.
- **Appendix A.3 - Declaration Files for Multi-language Character Sets**, used to describe the capabilities of an SGML system and is intended for human interpretation. The DCL files provide information on character encoding used in the DTD and the document, the amount of system resources required by the DTD, the delimiters used in marking up the document, the SGML features used by the document markup, and other application-specific information.

To support the multi-language character set capability and to allow for the population of data in multiple languages in a single SGML message, several SGML declaration files are included in the distribution of the ICH ICSR DTD. The correct SGML declaration file must be selected along with the ICH ICSR DTD and the ICH ICSR SGML instance, to correctly parse an ICH ICSR message. The method by which an SGML parser is told to use a specific declaration is parser specific. Appendix A.3 lists the five DCL files that have been included in the distribution of ICH ICSR version 2.0. These DCL files are also to be used in a similar manner when preparing the ICSR Acknowledgment Messages.

- **Appendix A.4 - ICH M2 Numeric Codes for Unit List**, used to populate fields that require the E2B unit list, documented in Attachment 1 of the E2B document. The three digit ICH M2 numeric codes represent unit measurements for mass, volume, radioactivity, other units, and unit intervals.

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- **Appendix A.5 - ICH M2 Numeric Codes for Routes of Administration**, used to populate fields that require the E2B Routes of Administration, documented in Attachment 2 of the E2B document. The M2 numeric codes represent various pre-defined routes of administration.

The references below help those receiving, validating, and acknowledging ICH ICSRs prepare ICSR Acknowledgment Messages:

- **Appendix A.6 - Requirements for the ICSR Acknowledgment Message**, used to verify the field name, description, DTD descriptor, field length, and field value for each data element of the ICSR Acknowledgment Message. In addition, this document is used to verify repeatable blocks and communicate to the sender of the ICSR message the results of the validation of the transmitted data set. This list of data element requirements must be used to verify the accuracy and compliance of data entered when preparing an ICSR Acknowledgment Message.
- **Appendix A.7 - ICH ICSR Acknowledgment DTD**, used to describe the SGML specifications of the elements and relationships of the acknowledgment message being transmitted. Within the encoded text, the DTD specifies which elements are required and where they may appear, as well as their order of appearance.
- **Appendix A.8 - Sample SGML Data File for the ICH ICSR Acknowledgment DTD**, used to provide an example of a valid SGML data file. This example represents a usable ICSR Acknowledgment SGML message that complies with ICSR Acknowledgment DTD, as well as the requirements specified for an acknowledgment message.
- **Appendix A.9 - Agreement on Unique Identifier**, used to identify ICSRs transmitted from companies to other companies, companies to authorities, and between authorities. M2 has referenced the E2B Step 4 document to derive an explicit technical solution for uniquely identifying reports, resulting in amendments to the following fields: A.1.10.1 National regulatory authority's case report number, A.1.10.2 Company's case report number, and A.1.10.3 Other sender's case report number.

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**A.1 ICSR Attribute List (Ver 4.4, 02/22/99, E2bs4v44.doc)**

Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
<b>ICH ICSR Message Header Specifications</b>					
M.1	ICH ICSR Message Header	Header/Entity			ichicsrmessagename
M.1.1	Message Type	Type of information being transmitted	16AN	ichicsr	messagetype
M.1.2	Message Format Version	Version number of Message Format	3AN		messageformatversion
M.1.3	Message Format Release	Release number of the Message Format	3AN		messageformatrelease
M.1.4	Message Number	Message Number	100AN		messagenumb
M.1.5	Message Sender Identifier	Message Sender Identifier	60AN		messagesenderidentifier
M.1.6	Message Receiver Identifier	Message Receiver Identifier	60AN		messagereceiveridentifier
M.1.7a	Message Date	Message Date Format (include as an attribute)	3N	204 – Format CCYYMMDDHHMMSS	messagedateformat
M.1.7b	Message Date	Message Date	14N	CCYYMMDDHHMMSS	messagedate
<b>ICH ICSR M2 Data Processing Specifications</b>					
	Safety Report Identifier	Safety Report Identifier	100AN		safetyreportid
	Safety Report Version Number	Safety Report Version Number	2AN		safetyreportversion
<b>E2B Step 4 Specifications</b>					
A.1	Identification of the case safety report	Header/entity			safetyreport
A.1.1	Identification of the country of the primary		2A	ISO3166	primarysourcecountry
A.1.2	Identification of the country where the reaction/event occurred		2A	ISO3166	occurcountry
A.1.3a	Date of this transmission	Date format	3N	102 - Format CCYYMMDD	transmissiondateformat

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.1.3b	Date of this transmission		8N	CCYYMMDD	transmissiondate
A.1.4	Type of report		1N	1=Spontaneous 2=Report from study 3=Other 4=Not available to sender (unknown)	reporttype
A.1.5	Seriousness	Header			
A.1.5.1	Serious		1N	1=Yes 2=No	serious
A.1.5.2	Seriousness criteria	Results in death	1N	1=Yes 2=No	seriousnessdeath
		Life threatening	1N	1=Yes 2=No	seriousnesslifethreatening
		Caused/prolonged hospitalization	1N	1=Yes 2=No	seriousnesshospitalization
		Disabling/Incapacitating	1N	1=Yes 2=No	seriousnessdisabling
		Congenital anomaly/birth defect	1N	1=Yes 2=No	seriousnesscongenitalanomaly
		Other medically important condition	1N	1=Yes 2=No	seriousnessother
A.1.6a	Date report was first received from source	Date format	3N	102 - Format CCYYMMDD	receivedateformat
A.1.6b	Date report was first received from source		8N	CCYYMMDD	receivedate
A.1.7a	Date of receipt of the most recent information for this report	Date format	3N	102 - Format CCYYMMDD	receiptdateformat
A.1.7b	Date of receipt of the most recent information for this report		8N	CCYYMMDD	receiptdate
A.1.8	Additional available documents held by sender	Header			
A.1.8.1	Are additional documents available		1N	1=Yes 2=No	additionaldocument
A.1.8.2	List of documents held by sender		100AN		documentlist
A.1.9	Does this case fulfill the local criteria for an expedited report?		1N	1=Yes 2=No	fulfillexpeditecriteria

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.1.10	Report identification number(s)	Header			
A.1.10.1	National regulatory authority's case report number		100AN		authoritynumb
A.1.10.2	Company's case report number		100AN		companynumb
A.1.10.3	Other sender's case report number		100AN		othernumb
A.1.11	Suspected duplicate		1N	1=Yes	duplicate
	entity				<b>reportduplicate</b>
A.1.11.1	Source of the duplicate		50AN	Should be a repeatable block	duplicatesource
A.1.11.2	Case report number of the suspected duplicate		100AN	Should be a repeatable block	duplicatenumb
	entity				<b>linkedreport</b>
A.1.12	Identification number of the report which is linked to this report		100AN	Should be a repeatable field	linkreportnumb
	entity				<b>(safetyreport)</b>
A.1.13	Report nullification		1N	1=Yes	casenullification
A.1.13.1	Reason for nullification		200AN		nullificationreason
A.1.14	Was the case medically confirmed, if not initially from health professional?		1N	1=Yes 2=No	medicallyconfirm
A.2	Primary source(s) of information	Header/entity		Area below should be a repeatable block	<b>primarysource</b>
A.2.1	Primary source(s)	Header			
A.2.1.1a	Reporter identifier	Reporter title	10AN		reportertitle
A.2.1.1b	Reporter identifier	Reporter given name	35AN		reportergivenname
A.2.1.1c	Reporter identifier	Reporter middle name	15AN		reportermiddlename
A.2.1.1d	Reporter identifier	Reporter family name	35AN		reporterfamilyname
A.2.1.2a	Reporter identifier	Reporter organization	60AN		reporterorganization
A.2.1.2b	Reporter identifier	Reporter department	60AN		reporterdepartment

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.2.1.2c	Reporter's address	Reporter street	60AN		reporterstreet
A.2.1.2d	Reporter's address	Reporter city	35AN		reportercity
A.2.1.2e	Reporter's address	Reporter state or province	40AN		reporterstate
A.2.1.2f	Reporter's address	Reporter postcode	15AN		reporterpostcode
A.2.1.3	Country	Reporter country code	2A	ISO3166	reportercountry
A.2.1.4	Qualification		1N	1=Physician 2=Pharmacist 3=Other Health Professional 4=Lawyer 5=Consumer or other non health professional	qualification
A.2.2	Literature reference(s)		500 AN		literaturereference
A.2.3	Study identification	Header			
A.2.3.1	Study name		100AN		studyname
A.2.3.2	Sponsor study number		35AN		sponsorstudynumb
A.2.3.3	Study type in which the reactions/events were observed		1N	1=Clinical trials 2=Individual patient use 3=Other studies	observestudytype
A.3	Information on sender and receiver of Case Safety Report	Header			
A.3.1	Sender	Header/entity			sender
A.3.1.1	Type		1N	1=Pharmaceutical Company 2=Regulatory Authority 3=Health professional 4=Regional Pharmacovigilance Center 5=WHO Collaborating Center for International Drug Monitoring 6=Other	sendertype
A.3.1.2	Sender Identifier	Sender organization	60AN		senderorganization
A.3.1.3a	Sender Identifier	Sender department	60AN		senderdepartment
A.3.1.3b	Sender Identifier	Title	10AN		sendertitle
A.3.1.3c	Sender Identifier	Given name	35AN		sendergivename

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.3.1.3d	Sender Identifier	Middle name	15AN		sendermiddlename
A.3.1.3e	Sender Identifier	Family name	35AN		senderfamilyname
A.3.1.4a	Sender's Address	Street address	40AN		senderstreetaddress
A.3.1.4b	Sender's Address	City	35AN		sendercity
A.3.1.4c	Sender's Address	State or Province	40AN		senderstate
A.3.1.4d	Sender's Address	Postcode	15AN		senderpostcode
A.3.1.4e	Sender's Address	Country Code	2A	ISO3166	sendercountrycode
A.3.1.4f	Sender's Telephone Number	Telephone	10AN		sendertel
A.3.1.4g	Sender's Telephone Number	Telephone extension	5AN		senderteleextension
A.3.1.4h	Sender's Telephone Number	Telephone country code	3AN		sendertelcountrycode
A.3.1.4i	Sender's Fax Number	Fax	10AN		senderfax
A.3.1.4j	Sender's Fax Number	Fax extension	5AN		senderfaxextension
A.3.1.4k	Sender's Fax Number	Fax country code	3AN		senderfaxcountrycode
A.3.1.4l	Sender's E-mail Address	E-mail address	100AN		senderemailaddress
A.3.2	Receiver	Header/entity			<b>receiver</b>
A.3.2.1	Type		1N	1=Pharmaceutical Company 2=Regulatory Authority 4=Regional Pharmacovigilance Center 5=WHO Collaborating Center for International Drug Monitoring 6=Other	receivertype
A.3.2.2a	Receiver identifier	Receiver organization	60AN		receiverorganization
A.3.2.2b	Receiver identifier	Receiver department	60AN		receiverdepartment

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
A.3.2.2c	Receiver identifier	Title	10AN		receivertitle
A.3.2.2d	Receiver identifier	Given name	35AN		receivergivenname
A.3.2.2e	Receiver identifier	Middle name	15AN		receivermiddle name
A.3.2.2f	Receiver identifier	Family name	35AN		receiverfamilyname
A.3.2.3a	Receiver's Address	Street address	40AN		receiverstreetaddress
A.3.2.3b	Receiver's Address	City	35AN		receivercity
A.3.2.3c	Receiver's Address	State or Province	40AN		receiverstate
A.3.2.3d	Receiver's Address	Postcode	15AN		receiverpostcode
A.3.2.3e	Receiver's Address	Country Code	2A	ISO3166	receivercountrycode
A.3.2.3f	Receiver's Telephone Number	Telephone	10AN		receivertel
A.3.2.3g	Receiver's Telephone Number	Telephone extension	5AN		receiverteleextension
A.3.2.3h	Receiver's Telephone Number	Telephone country code	3AN		receivertelcountrycode
A.3.2.3i	Receiver's Fax Number	Fax	10AN		receiverfax
A.3.2.3j	Receiver's Fax Number	Fax extension	5AN		receiverfaxextension
A.3.2.3k	Receiver's Fax Number	Fax country code	3AN		receiverfaxcountrycode
A.3.2.3l	Receiver's E-mail Address	E-mail address	100AN		receiveremailaddress
B	Information on Case	Header			
B.1	Patient characteristics	Header/entity			<b>patient</b>
B.1.1	Patient initials		10AN		patientinitial

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.1.1a	Patient medical record number(s) and source(s)	GP medical record number	20AN		patientgpmmedicalrecordnumb
B.1.1.1b	Patient medical record number(s) and source(s)	Specialist record number	20AN		patientspecialistrecordnumb
B.1.1.1c	Patient medical record number(s) and source(s)	Hospital record number	20AN		patienthospitalrecordnumb
B.1.1.1d	Patient medical record number(s) and source(s)	Investigation number	20AN		patientinvestigationnumb
B.1.2	Age information	Header			
B.1.2.1a	Date of birth	Date format	3N	102 - Format CCYYMMDD	patientbirthdateformat
B.1.2.1b	Date of birth		8N	CCYYMMDD	patientbirthdate
B.1.2.2a	Age at time of onset of reaction/event	Age value	5N		patientonsetage
B.1.2.2b	Age at time of onset of reaction/event	Age unit	3N	800 = Decade 801=Year 802=Month 803=Week 804=Day 805=Hour	patientonsetageunit
B.1.2.2.1a	Gestation period when reaction/event was observed in the fetus	Gestation period when reaction/event was observed in the fetus	3N		gestationperiod
B.1.2.2.1b	Gestation period when reaction/event was observed in the fetus unit	Unit	3N	802=Month 803=Week 804=Day 810=Trimester	gestationperiodunit
B.1.2.3	Patient age group		1N	1=Neonate 2=Infant 3=Child 4=Adolescent 5=Adult 6=Elderly	patientagegroup
B.1.3	Weight (kg)		6N		patientweight
B.1.4	Height (cm)		3N		patientheight

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.5	Sex		1N	ISO 5218 1=Male 2=Female 9 =Not specified 0=Unknown	patientsex
B.1.6a	Last menstrual period date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	lastmenstrualdateformat
B.1.6b	Last menstrual period date		8N		patientlastmenstrualdate
B.1.7	Relevant medical history and concurrent conditions	Header		Area below should be a repeatable block	<b>medicalhistoryepisode</b>
B.1.7.1a	Structured information	Disease / surgical procedure / etc.	100AN		patientmedicalepisodename
B.1.7.1b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientmedicalstartdateformat
B.1.7.1c	Start Date		8N		patientmedicalstartdate
B.1.7.1d	Continuing		1N	1=Yes 2=No 3=Unknown	patientmedicalcontinue
B.1.7.1e	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientmedicalenddateformat
B.1.7.1f	End Date		8N		patientmedicalenddate
B.1.7.1g	Comments		100AN		patientmedicalcomment
		entity			<b>(patient)</b>
B.1.7.2	Text for relevant medical history and concurrent conditions		2000AN		patientmedicalhistorytext
B.1.8	Relevant past drug history (repeat as necessary)	Header/entity		Area below should be a repeatable block	<b>patientpastdrugtherapy</b>
B.1.8a	Name of Drug as Reported		70AN		patientdrugname

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.8b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdrugstartdateformat
B.1.8c	Start Date		8N		patientdrugstartdate
B.1.8d	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdrugenddateformat
B.1.8e	End Date		8N		patientdrugenddate
B.1.8f	Indication		100AN		patientdrugindication
B.1.8g	Reaction		100AN		patientdrugreaction
B.1.9	In case of death:	Header/entity			<b>patientdeath</b>
B.1.9.1a	Date of death	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	patientdeathdateformat
B.1.9.1b	Date of death		8N		patientdeathdate
		entity			<b>patientdeathcause</b>
B.1.9.2	Reported cause of death (repeat as necessary)		100AN	Should be a repeatable field	patientdeathreport
		entity			<b>(patientdeath)</b>
B.1.9.3	Was autopsy done?		1N	1=Yes 2=No 3=Unknown	patientautopsyyesno
		entity			<b>patientautopsy</b>
B.1.9.4	Autopsy-determined cause(s) of death (repeat as necessary)		100AN	Should be a repeatable field	patientdetermineautopsy
B.1.10	For a parent-child/fetus report, information concerning the parent:	Header/entity			<b>parent</b>
B.1.10.1	Parent identification	Parent initials	10AN		parentidentification
B.1.10.2	Parent age information	Header			
B.1.10.2.1a	Date of birth of parent	Date format	3N	102 – Format CCYYMMDD	parentbirthdateformat
B.1.10.2.1b	Date of birth of parent		8N	CCYYMMDD	parentbirthdate
B.1.10.2.2a	Age of parent	Age Value	2N		parentage

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.1.10.2.2b	Age of parent	Age unit	3N	801=Year	parentageunit
B.1.10.3a	Last menstrual period date	Date format	3N	102 – Format CCYYMMDD	parentlastmenstrualdateformat
B.1.10.3b	Last menstrual period date		8N	CCYYMMDD	parentlastmenstrualdate
B.1.10.4	Weight (kg) of parent		6N		parentweight
B.1.10.5	Height (cm) of parent		3N		parentheight
B.1.10.6	Sex of parent		1N	ISO 5218 1=Male 2=Female 9=Not Specified 0=Unknown	parentsex
B.1.10.7	Relevant medical history and concurrent conditions of parent	Header/entity		Area below should be a repeatable block	<b>parentmedicalhistoryepisode</b>
B.1.10.7.1a	Structured information	Disease / surgical procedure/ etc.	100AN		parentmedicalepisodename
B.1.10.7.1b	Start Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentmedicalstartdateformat
B.1.10.7.1c	Start Date		8N		parentmedicalstartdate
B.1.10.7.1d	Continuing		1N	1=Yes 2=No 3=Unknown	parentmedicalcontinue
B.1.10.7.1e	End Date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentmedicalenddateformat
B.1.10.7.1f	End Date		8N		parentmedicalenddate
B.1.10.7.1g	Comments		100AN		parentmedicalcomment
		entity			<b>(parent)</b>
B.1.10.7.2	Text for relevant medical history and concurrent conditions (not including reaction/event) of parent		500AN		parentmedicalrelevanttext
B.1.10.8	Relevant past drug history	Header/entity		Area below should be a repeatable block	<b>parentpastdrugtherapy</b>
B.1.10.8a	Name of drug as		70AN		parentdrugname

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
	reported				
B.1.10.8b	Start date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentdrugstartdateformat
B.1.10.8c	Start date		8N		parentdrugstartdate
B.1.10.8d	End date	Date format	3N	102 - Format CCYYMMDD, 610 - Format CCYYMM, 602 - Format CCYY	parentdrugenddateformat
B.1.10.8e	End date		8N		parentdrugenddate
B.1.10.8f	Indication		100AN		parentdrugindication
B.1.10.8g	reactions (if any and known)		100AN		parentdrugreaction
B.2	Reaction(s)/Event(s)	Header/entity		Area below should be a repeatable block	<b>reaction</b>
B.2.i.1	Reaction/event as reported by primary source		100AN		primarysourceraction
B.2.i.2	Reaction/event term		100AN		reactionterm
B.2.i.3	Term highlighted by the reporter		1N	1=Yes	termhighlighted
B.2.i.4a	Date of start of reaction/event	Date format	3N	102 - Format CCYYMMDD, 203 - Format CCYYMMDDHHMM, 610 - Format CCYYMM, 602 - Format CCYY	reactionstartdateformat
B.2.i.4b	Date of start of reaction/event		12N		reactionstartdate
B.2.i.5a	Date of end of reaction/event	Date format	3N	102 - Format CCYYMMDD, 203 - Format CCYYMMDDHHMM, 610 - Format CCYYMM, 602 - Format CCYY	reactionenddateformat
B.2.i.5b	Date of end of reaction/event		12N		reactionenddate
B.2.i.6a	Duration of reaction/event		5N		reactionduration

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.2.i.6b	Duration of reaction/event	Duration unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactiondurationunit
B.2.i.7.1a	Time interval between beginning of suspect drug administration and start of reaction/event		5N		reactionfirsttime
B.2.i.7.1b	Time interval unit between suspect drug administration and start of reaction/event	Time interval unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactionfirsttimeunit
B.2.i.7.2a	Time interval between last dose and start of reaction/event		5N		reactionlasttime
B.2.i.7.2b	Time interval unit between last dose and start of reaction/event	Time interval unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	reactionlasttimeunit
B.2.i.8	Outcome of reaction/event at the time of last observation		1N	1=recovered/resolved 2=recovering/resolving 3=not recovered/not resolved 4=recovered/resolved with sequel 5=fatal 6=unknown	reactionoutcome
B.3	Results of tests and procedures relevant to the investigation of the patient:	Header/entity		Area below should be a repeatable block	test
B.3.1a	Structured information (repeat as necessary)	Date format	3N	102 - Format CCYYMMDD, 610 - Format	testdateformat

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				CCYYMM, 602 - Format CCYY	
B.3.1b	Date		8N		testdate
B.3.1c	Test		70AN		testname
B.3.1d	Result		10AN		testresult
B.3.1e	Unit		35AN		testunit
B.3.1.1	Normal Low range		10AN		lowtestrange
B.3.1.2	Normal High Range		10AN		hightestrange
B.3.1.3	More Information Available (Y/N)		1N	1=Yes 2= No	moreinformation
		entity			(patient)
B.3.2	Results of tests and procedures relevant to the investigation of the patient:		2000AN		resultstestsprocedures
B.4	Drug(s) Information	Header/entity		Area below should be a repeatable block	<b>drug</b>
B.4.k.1	Characterization of drug role		1N	1=Suspect 2=Concomitant 3=Interacting	drugcharacterization
B.4.k.2	Drug identification	Header			
B.4.k.2.1	Proprietary medicinal product name		70AN		medicinalproduct
		entity			<b>activesubstance</b>
B.4.k.2.2	Active Drug substance names		70AN		activesubstancename
		entity			<b>(drug)</b>
B.4.k.2.3	Identification of the country where the drug was obtained		2A	ISO3166	obtaindrugcountry
B.4.k.3	Batch/lot number		35AN		drugbatchnumb
B.4.k.4	Holder and authorization/application number of drug	Header			
B.4.k.4.1	Authorization/Application Number		35AN		drugauthorizationnumb
B.4.k.4.2	Country of authorization/application		2A	ISO3166	drugauthorizationcountry
B.4.k.4.3	Name of holder/applicant		60AN		drugauthorizationholder

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.5	Structured Dosage Information:	Header			
B.4.k.5.1	dose (number)		8N		drugstructuredosagenumb
B.4.k.5.2	dose (unit)		3N	001=kg kilogram(s) 002=G gram(s) 003=Mg milligram(s) 004=µg microgram(s) 005=ng nanogram(s) 006=pg picogram(s) 007=mg/kg milligram(s)/kilogram 008=µg/kg microgram(s)/kilogram 009=mg/m <sup>2</sup> milligram(s)/sq. meter 010=µg/m <sup>2</sup> microgram(s)/ sq. Meter 011=l litre(s) 012=ml millilitre(s) 013=µl microlitre(s) 014=Bq becquerel(s) 015=GBq gigabecquerel(s) 016=MBq megabecquerel(s) 017=Kbq kilobecquerel(s) 018=Ci curie(s) 019=MCi millicurie(s) 020=µCi microcurie(s) 021=NCi nanocurie(s) 022=Mol mole(s) 023=Mmol millimole(s) 024=µmol micromole(s) 025=IU international unit(s) 026=Kiu iu(1000s) 027=Miu iu(1,000,000s) 028=iu/kg iu/kilogram 029=Meq milliequivalent(s) 030=% percent 031=Gtt drop(s) 032=DF dosage form	drugstructuredosageunit
B.4.k.5.3	number of separate dosages		3N		drugseparatedosagenumb

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.5.4	number of units in the interval		3N		drugintervaldosageunitnumb
B.4.k.5.5	definition of the interval		3AN		drugintervaldosagedefinition
B.4.k.5.6	cumulative dose to first reaction (number)		10N		drugcumulativedosagenumb
B.4.k.5.7	cumulative dose to first reaction (unit)		3AN		drugcumulativedosageunit
B.4.k.6	Dosage text		100AN		drugdosagetext
B.4.k.7	Pharmaceutical form (Dosage form)		50AN		drugdosageform
B.4.k.8	Route of administration		3N	001 = Auricular (otic) 002 = Buccal 003 = Cutaneous 004 = Dental 005 = Endocervical 006 = Endosinusial 007 = Endotracheal 008 = Epidural 009 = Extra-amniotic 010 = Hemodialysis 011 = Intra corpus cavernosum 012 = Intra-amniotic 013 = Intra-arterial 014 = Intra-articular 015 = Intra-uterine 016 = Intracardiac 017 = Intracavernous 018 = Intracerebral 019 = Intracervical 020 = Intracisternal 021 = Intracorneal 022 = Intracoronary 023 = Intradermal 024 = Intradiscal (intraspinal) 025 = Intrahepatic 026 = Intralesional 027 = Intralymphatic 028 = Intramedullar (bone marrow) 029 = Intrameningeal 030 = Intramuscular 031 = Intraocular	drugadministrationroute

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				032 = Intrapericardial 033 = Intraperitoneal 034 = Intrapleural 035 = Intrasynovial 036 = Intratumor 037 = Intrathecal 038 = Intrathoracic 039 = Intratracheal 040 = Intravenous bolus 041 = Intravenous drip 042 = Intravenous (not otherwise specified) 043 = Intravesical 044 = Iontophoresis 045 = Nasal 046 = Occlusive dressing technique 047 = Ophthalmic 048 = Oral 049 = Oropharyngeal 050 = Other 051 = Parenteral 052 = Periarticular 053 = Perineural 054 = Rectal 055 = Respiratory (inhalation) 056 = Retrobulbar 057 = Sunconjunctival 058 = Subcutaneous 059 = Subdermal 060 = Sublingual 061 = Topical 062 = Transdermal 063 = Transmammary 064 = Transplacental 065 = Unknown 066 = Urethral 067 = Vaginal	
B.4.k.9	Parent route of administration (in case of a parent child/fetus report)		3N	001 = Auricular (otic) 002 = Buccal 003 = Cutaneous 004 = Dental 005 = Endocervical 006 = Endosinusial 007 = Endotracheal 008 = Epidural	drugparadministration

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				009 = Extra-amniotic 010 = Hemodialysis 011 = Intra corpus cavernosum 012 = Intra-amniotic 013 = Intra-arterial 014 = Intra-articular 015 = Intra-uterine 016 = Intracardiac 017 = Intracavernous 018 = Intracerebral 019 = Intracervical 020 = Intracisternal 021 = Intracorneal 022 = Intracoronal 023 = Intradermal 024 = Intradiscal (intraspinous) 025 = Intrahepatic 026 = Intralesional 027 = Intralymphatic 028 = Intramedullar (bone marrow) 029 = Intrameningeal 030 = Intramuscular 031 = Intraocular 032 = Intrapericardial 033 = Intraperitoneal 034 = Intrapleural 035 = Intrasynovial 036 = Intratumor 037 = Intrathecal 038 = Intrathoracic 039 = Intratracheal 040 = Intravenous bolus 041 = Intravenous drip 042 = Intravenous (not otherwise specified) 043 = Intravesical 044 = Iontophoresis 045 = Nasal 046 = Occlusive dressing technique 047 = Ophthalmic 048 = Oral 049 = Oropharyngeal 050 = Other	

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
				051 = Parenteral 052 = Periarticular 053 = Perineural 054 = Rectal 055 = Respiratory (inhalation) 056 = Retrobulbar 057 = Sunconjunctival 058 = Subcutaneous 059 = Subdermal 060 = Sublingual 061 = Topical 062 = Transdermal 063 = Transmammary 064 = Transplacental 065 = Unknown 066 = Urethral 067 = Vaginal	
B.4.k.10a	Gestation period at time of exposure		3N		reactiongestationperiod
B.4.k.10b	Gestation period at time of exposure	Gestation period unit	3N	802=Month 803=Week 804=Day 810=Trimester	reactiongestationperiodunit
B.4.k.11	Indication for use in the case		100AN		drugindication
B.4.k.12a	Date of start of drug	Date format	3N	102 – Format CCYYMMDD, 610 – Format CCYYMM, 602 - Format CCYY	drugstartdateformat
B.4.k.12b	Date of start of drug		8N		drugstartdate
B.4.k.13	Time interval between drug administration and start of reaction/event	Header			
B.4.k.13.1a	Time interval between beginning of drug administration and start of reaction/event		5N		drugstartperiod

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
B.4.k.13.1b	Time interval between beginning of drug administration and start of reaction/event	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	drugstartperiodunit
B.4.k.13.2a	Time interval between last dose of drug and start of reaction/event		5N		druglastperiod
B.4.k.13.2b	Time interval between beginning of drug administration and start of reaction/event	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute 807=Second	druglastperiodunit
B.4.k.14a	Date of last administration	Date format	3N	102 – Format CCYYMMDD, 610 – Format CCYYMM, 602 - Format CCYY	drugenddateformat
B.4.k.14b	Date of last administration		8N		drugenddate
B.4.k.15a	Duration of drug administration		5N		druttreatmentduration
B.4.k.15b	Duration of drug administration unit	Time unit	3N	801=Year 802=Month 803=Week 804=Day 805=Hour 806=Minute	druttreatmentdurationunit
B.4.k.16	Action(s) taken with drug		1N	1=Drug withdrawn 2=Dose reduced 3=Dose increased 4=Dose not changed 5=Unknown 6=Not applicable	actiondrug
B.4.k.17	Effect of rechallenge (or re-exposure), for suspect drugs only	Header			
B.4.k.17.1	Did reaction recur on readministration?		1N	1=Yes 2= No 3 = Unknown	drugrecurreadministration

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Data Element	Title	Description	Field Length	Field Value	DTD Descriptor
		entity			<b>drugrecurrence</b>
B.4.k.17.2	If yes, which reaction/event recurred?		100AN		drugrecuraction
B.4.k.18	Relatedness of drug to reaction/event (repeat as necessary)	Header/entity			<b>drugreactionrelatedness</b>
B.4.k.18.1	Reaction assessed		100AN		drugreactionasses
B.4.k.18.2	Source of assessment		60AN		drugassessmentsource
B.4.k.18.3	Method of assessment		35AN		drugassessmentmethod
B.4.k.18.4	Result		35AN		drugresult
		entity			<b>(drug)</b>
B.4.k.19	Additional information on drug		100AN		drugadditional
B.5	Narrative case summary and further information:	Header/entity			<b>summary</b>
B.5.1	Case narrative including clinical course, therapeutic measures, outcome and additional relevant information.		10,000 AN		narrativeincludclinical
B.5.2	Reporter's comments		210AN		reportercomment
B.5.3	Sender's diagnosis/syndrome and/or reclassification of reaction/event		210AN		senderdiagnosis
B.5.4	Sender's comments		1,000AN		sendercomment

The following list describes the data types specified in the field length column of the attribute list:

**A - Alpha:** This data type is primarily used within the ICSR for certain fields that require controlled vocabulary, such as A.1.1 Identification of the Country - 2A, to accommodate the ISO3166 code. The string fields that require the Alpha data type can contain only upper and lower case alphabetic characters, e.g. "en". Numbers and special characters, such as '.', '^' are not allowed.

**AN - AlphaNumeric:** String field that can contain alphabetic, numerical and special characters. Example: "AB-19.990115"."

**N - Numeric:** String field that contains only the characters "0-9.E+-" used to represent an integer or floating point numbers, including scientific notation. Example: "1.23E-1" or "34192" or "32.12".

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## A.2 ICH ICSR DTD (Document Type Definition)

```
<!DOCTYPE ichicsr [
<!-- PUBLIC "-//ICHM2//DTD ICH ICSR Vers. 2.0//EN" "ich-icsr-v2.0.dtd" -->
<!--
Individual Case Safety Report Document Type Definition
```

This DTD is issued by the ICH M2 group and is public domain in nature.

No one can claim copyright on this DTD.  
No commercial distribution is allowed.

The ICH is not responsible for any damage or financial loss resulting from use of this DTD. This version is tentative in nature and changes are expected. This DTD is subject to the ICH M2 change control procedures.

Version 1.0, Release 1.0, October 17, 1997

1998-04-21 Modifications made by JPMA

1. Changed "resultstestsprocedures" to "resultstestsprocedures?".
2. Spelling correction "seriousnesslifethreatning" to "seriousnesslifethreatening".
3. Spelling correction "seriousnessconginalanomali" to "seriousnesscongenitalanomali".
4. Changed ELEMENT "parentmedicalstructure" to "parentmedicalepisodenname".

1998-09-27 Modifications made by FDA

5. Added lang attribute to ichicsr as #REQUIRED using a %lang.att entity.
6. Added lang attribute to all other elements as #IMPLIED.
7. Removed all unordered "&" connectors and replaced with the ordered connector ",," to be compatible with XML.
8. Changed the names of elements under "ichicsrmessagenameheader" to comply with group decisions.
9. Removed all "old" elements.
10. Removed all sequence number entities.
11. Added Standard SGML character entities &lt;, &gt;, &amp; so that markup can be escaped as necessary.
12. Removed the %act.rec; and %ope.rec; internal entities, thus removing all support for the "(app | rep | del )" construct.
13. Root element of DTD is now "ichicsr" which allows one "ichicsrmessagenameheader" followed by "safetyreport+".

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14. The relationship between "drug" and "activesubstance" is now one to zero or many.

Version 2.0, Release 1.0, Date to be decided

-->

<!-- TECHNICAL NOTE

ICH ICSR SGML Declaration

To correctly parse an ICH ICSR SGML message requires the selection of the correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance. This technical note provides guidance on which of several SGML declarations included with the ICH ICSR application to select based on the language and character set used within the ICH ICSR SGML instance. The method by which an SGML parser is told to use a specific declaration is parser specific.

The three most common methods are -

1. Tell the parser via the command line which declaration to use.
2. Tell the parser via a specific environment variable which declaration to use.
3. If the parser supports SGML Open catalogs, within the catalog file is a command that can tell the parser which declaration to use. SGML catalog files are an industry standard way to tell a parser how to find all of the pieces (declaration, DTD, SGML document instance) needed to successfully parse.

To cover all of the languages necessary to support the ICH ICSR application, ISO 10646 (UNICODE) would have to be used. If this were the case, then only one SGML declaration would be needed to support all ICH ICSR languages. Because UNICODE support is not available in all popular computer application programs, the ICH M2 EWG has recommended that a variety of character sets be used at this time, instead of a single UNICODE character encoding. For each of these different character encodings a different SGML declaration needs to be generated and used.

Five SGML declarations are included with the ICH ICSR distribution. They are described briefly below.

ich-icsr-latin1.dcl - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

ich-icsr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

ich-icsr-sjis.dcl - This SGML declaration supports the Shift JIS character set for encoding Japanese.

ich-icsr-utf8.dcl - This SGML declaration supports the ISO 10646 (UNICODE) UTF-8 character set. This character set supports almost all of the worlds currently written languages.

ich-icsr-mult.dcl - This SGML declaration will support all of the currently defined ICHICSR languages, and it doesn't require the use of UNICODE. It is however a "hack" that relies on a fortuitous characteristic of the languages currently being used within the ICH ICSR SGML application.

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This hack works because the character set documented within an SGML declaration is for the benefit of both the SGML parser, and the programmer who implements the SGML application. The programmer needs detailed knowledge of all the characters being used to correctly code an application. The parser only really needs to about some of the characters. In particular it needs to know which characters signify an SGML event. For instance that the "<" character starts an SGML open tag, and the "</" character sequence starts an SGML close tag. All told, the parser needs to know very little. Because of the particular combination of character sets being used within the ICH ICSR application, an SGML declaration can be defined that tells the parser just what it needs to know and still work across all of the different character sets. The catch is that this SGML declaration doesn't tell the programmer all that she or he needs to know to correctly code the rest of the application. If this declaration is used, the programmer will have to get this detailed information from another source.

```
-->

<! -- ===== -->
<! -- Entities -->
<! -- ===== -->

<! -- Use the lang attribute to indicate the language of an elements --
-- content via an ISO 639 language Code. -->

<!ENTITY % lang.att "lang CDATA #IMPLIED">

<! -- Standard Character Entities to escape SGML special characters. --
-- When "<", ">", and "&" occur in text, they should be replaced --
-- by "&lt;", "&gt;", and "&amp;" respectively. -->

<! -- Less Than "<" -->
<!ENTITY lt      "&#38;#60;">

<! -- Greater Than ">" -->
<!ENTITY gt      "&#62;">

<! -- Ampersand "&" -->
<!ENTITY amp     "&#38;#38;">

<! -- ===== -->
<! -- Elements and Attributes -->
<! -- ===== -->

<!ELEMENT ichicsr          - - (ichicsrmessagenameheader, safetyreport+)>
<!ATTLIST ichicsr
      lang   CDATA #REQUIRED
>

<! -- M.1 ICH ICSR Message Header Information -->

<!ELEMENT ichicsrmessagenameheader      - -
      (messagetype
       messageformatversion
       messageformatrelease
       messagenumb
       messagesenderidentifier
       ,
```

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```
messagereceiveridentifier      ,  
    messagedateformat  
    messagedate) >  
<!ATTLIST ichicsrmessagelheader  
    %lang.att;  
>  
  
<!-- M.1.1 Message Type -->  
<!ELEMENT messagetype          - - (#PCDATA) >  
<!ATTLIST messagetype  
    %lang.att;  
>  
  
<!-- M.1.2 Message Format Version -->  
<!ELEMENT messageformatversion - - (#PCDATA) >  
<!ATTLIST messageformatversion  
    %lang.att;  
>  
  
<!-- M.1.3 Message Format Release -->  
<!ELEMENT messageformatrelease - - (#PCDATA) >  
<!ATTLIST messageformatrelease  
    %lang.att;  
>  
  
<!-- M.1.4 Message Number -->  
<!ELEMENT messagenumb         - - (#PCDATA) >  
<!ATTLIST messagenumb  
    %lang.att;  
>  
  
<!-- M.1.5 Message Sender Identifier -->  
<!ELEMENT messagesenderidentifier - - (#PCDATA) >  
<!ATTLIST messagesenderidentifier  
    %lang.att;  
>  
  
<!-- M.1.6 Message Receiver Identifier -->  
<!ELEMENT messagereceiveridentifier - - (#PCDATA) >  
<!ATTLIST messagereceiveridentifier  
    %lang.att;  
>  
  
<!-- M.1.7a Message Date Format -->  
<!ELEMENT messagedateformat     - -      (#PCDATA) >  
<!ATTLIST messagedateformat  
    %lang.att;  
>  
  
<!-- M.1.7b Message Date -->  
<!ELEMENT messagedate      - -      (#PCDATA) >  
<!ATTLIST messagedate  
    %lang.att;  
>  
  
<!-- Individual Case Safety Report(s) Specifications -->  
<!-- A.1 Identification of the case safety report -->
```

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```
<!ELEMENT safetyreport      - -  
      (safetyreportid?,  
       safetyreportversion?,  
       primarysourcecountry?  
       occurcountry?  
       transmissiondateformat?  
       transmissiondate?  
       reporttype?  
       serious?  
       seriousnessdeath?  
       seriousnesslifethreatening?  
       seriousnesshospitalization?  
       seriousnessdisabling?  
       seriousnesscongenitalanomaly?  
       seriousnessother?  
       receivedateformat?  
       receivedate?  
       receiptdateformat?  
       receiptdate?  
       additionaldocument?  
       documentlist?  
       fulfillexpeditecriteria?  
       authoritynumb?  
       companynumb?  
       othernumb?  
       duplicate?  
       casenullification?  
       nullificationreason?  
       medicallyconfirm?  
           (reportduplicate*  
            linkedreport*  
            primarysource+  
            sender  
            receiver  
            patient))>  
<!ATTLIST safetyreport  
      %lang.att;  
>  
  
<!ELEMENT reportduplicate    - -  
      (duplicatesource?  
       duplicatenumb?)>  
<!ATTLIST reportduplicate  
      %lang.att;  
>  
  
<!ELEMENT linkedreport      - -      (linkreportnumb?)>  
<!ATTLIST linkedreport  
      %lang.att;  
>  
  
<!-- A.2 Primary source(s) of information -->  
<!ELEMENT primarysource     - -  
      (reportertitle?  
       reportergivenname?  
       reportermiddleinitial?
```

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```
reporterfamilyname?           ,
reporterorganization?         ,
reporterdepartment?          ,
reporterstreet?              ,
reportercity?                ,
reporterstate?               ,
reporterpostcode?             ,
reportercountry?             ,
qualification?               ,
literaturereference?         ,
studyname?                  ,
sponsorstudynumb?            ,
observestudytype?) >
<!ATTLIST primarysource
      %lang.att;
>

<!-- A.3.1 Sender --&gt;
&lt;!ELEMENT sender
      (sendertype?
       senderorganization?
       senderdepartment?
       sendertitle?
       sendergivenname?
       sendermiddle name?
       senderfamilyname?
       senderstreetaddress?
       sendercity?
       senderstate?
       senderpostcode?
       sendercountrycode?
       sendertel?
       sendertelextension?
       sendertelcountrycode?
       senderfax?
       senderfaxextension?
       senderfaxcountrycode?
       senderemailaddress?) &gt;
&lt;!ATTLIST sender
      %lang.att;
&gt;

<!-- A.3.2 Receiver --&gt;
&lt;!ELEMENT receiver
      (receivertype?
       receiverorganization?
       receiverdepartment?
       receivertitle?
       receivergivenname?
       receivermiddle name?
       receiverfamilyname?
       receiverstreetaddress?
       receivercity?
       receiverstate?
       receiverpostcode?
       receivercountrycode?
       receivertel?
       ,</pre>
```

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```
receiverteleextension? ,  
receivertelcountrycode? ,  
receiveverfax? ,  
receiveverfaxextension? ,  
receiveverfaxcountrycode? ,  
receiveveremailaddress?)>  
<!ATTLIST receiver  
    %lang.att;  
>  
  
<!-- B.1 Patient characteristics -->  
<!ELEMENT patient - -  
    (patientinitial?  
     patientgpmedicalrecordnumb?  
     patientspecialistrecordnumb?  
     patienthospitalrecordnumb?  
     patientinvestigationnumb?  
        patientbirthdateformat?  
     patientbirthdate?  
     patientonsetage?  
        patientonsetageunit?  
     gestationperiod?  
        gestationperiodunit?  
     patientagegroup?  
     patientweight?  
     patientheight?  
     patientsex?  
     lastmenstrualdateformat? ,  
     patientlastmenstrualdate?  
     patientmedicalhistorytext?  
     resultstestsprocedures?  
        (medicalhistoryepisode*  
         patientpastdrugtherapy*  
         patientdeath?  
         parent?  
         reaction+  
         test*  
         drug+  
         summary?))>  
<!ATTLIST patient  
    %lang.att;  
>  
  
<!-- B.1.7 Relevant medical history and concurrent -->  
<!ELEMENT medicalhistoryepisode - -  
    (patientmedicalepisodename?  
     patientmedicalstartdateformat? ,  
     patientmedicalstartdate?  
     patientmedicalcontinue?  
        patientmedicalenddateformat? ,  
     patientmedicalenddate?  
     patientmedicalcomment?)>  
<!ATTLIST medicalhistoryepisode  
    %lang.att;  
>  
  
<!-- B.1.8 Relevant past drug history -->
```

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```
<!ELEMENT patientpastdrugtherapy      - -  
      (patientdrugname?          ,  
       patientdrugstartdateformat? ,  
       patientdrugstartdate?      ,  
       patientdrugenddateformat? ,  
       patientdrugenddate?        ,  
       patientdrugindication?    ,  
       patientdrugreaction?)>  
  
<!ATTLIST patientpastdrugtherapy  
      %lang.att;  
>  
  
<!-- B.1.9 In case of death: -->  
<!ELEMENT patientdeath      - -  
      (patientdeathdateformat?      ,  
       patientdeathdate?          ,  
       patientautopsyyesno?        ,  
       (patientdeathcause*         ,  
        patientautopsy*))>  
<!ATTLIST patientdeath  
      %lang.att;  
>  
  
<!ELEMENT patientdeathcause      - -      (patientdeathreport?)>  
<!ATTLIST patientdeathcause  
      %lang.att;  
>  
  
<!ELEMENT patientautopsy      - -      (patientdetermineautopsy?)>  
<!ATTLIST patientautopsy  
      %lang.att;  
>  
  
<!-- B.1.10 For a parent-child / fetus report, information concerning the parent: - ->  
<!ELEMENT parent      - -  
      (parentidentification?          ,  
       parentbirthdateformat?        ,  
       parentbirthdate?            ,  
       parentage?                  ,  
       parentageunit?              ,  
       parentlastmenstrualdateformat? ,  
       parentlastmenstrualdate?      ,  
       parentweight?                ,  
       parentheight?               ,  
       parentsex?                  ,  
       parentmedicalrelevanttext?    ,  
       (parentmedicalhistoryepisode* ,  
        parentpastdrugtherapy*))>  
<!ATTLIST parent  
      %lang.att;  
>  
  
<!-- B.1.10.7 Relevant medical history and concurrent conditions of parent -->  
<!ELEMENT parentmedicalhistoryepisode - -
```

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```
(parentmedicalepisodename? ,  
 parentmedicalstartdateformat? ,  
 parentmedicalstartdate? ,  
 parentmedicalcontinue? ,  
 parentmedicalenddateformat? ,  
 parentmedicalenddate? ,  
 parentmedicalcomment?)>  
<!ATTLIST parentmedicalhistoryepisode  
 %lang.att;  
>  
  
<!-- B.1.10.8 Relevant past drug history -->  
<!ELEMENT parentpastdrugtherapy - -  
 (parentdrugname?  
 parentdrugstartdateformat?  
 parentdrugstartdate?  
 parentdrugenddateformat?  
 parentdrugenddate?  
 parentdrugindication?  
 parentdrugreaction?)>  
<!ATTLIST parentpastdrugtherapy  
 %lang.att;  
>  
  
<!-- B.2 Reaction(s) / Event(s) -->  
<!ELEMENT reaction - -  
 (primarysourcereaction?  
 reactionterm?  
 termhighlighted?  
 reactionstartdateformat?  
 reactionstartdate?  
 reactionenddateformat?  
 reactionenddate?  
 reactionduration?  
 reactiondurationunit?  
 reactionfirsttime?  
 reactionfirsttimeunit?  
 reactionlasttime?  
 reactionlasttimeunit?  
 reactionoutcome?)>  
<!ATTLIST reaction  
 %lang.att;  
>  
  
<!-- B.3 Results of tests and procedures relevant to the investigation of the  
 patient: -->  
<!ELEMENT test - -  
 (testdateformat?  
 testdate?  
 testname?  
 testresult?  
 testunit?  
 lowtestrange?  
 hightestrange?  
 moreinformation?)>  
<!ATTLIST test
```

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```
%lang.att;  
>  
  
<!ELEMENT drug      - -  
  (drugcharacterization?  
   medicinalproduct?      ,  
   obtaindrugcountry?     ,  
   drugbatchnumb?         ,  
   drugauthorizationnumb?  
   drugauthorizationcountry? ,  
   drugauthorizationholder? ,  
   drugstructuredosagenumb?  
   drugstructureddosageunit?  
   drugseparatedosagenumb?  
   drugintervaldosageunitnumb?  
   drugintervaldosagedefinition?  
   drugcumulativedosagenumb?  
   drugcumulativedosageunit?  
   drugdosagetext?  
   drugdosageform?  
   drugadministrationroute?  
   drugparadministration?  
   reactiongestationperiod?  
     reactiongestationperiodunit? ,  
   drugindication?  
     drugstartdateformat?  
   drugstartdate?  
   drugstartperiod?  
     drugstartperiodunit?  
   druglastperiod?  
     druglastperiodunit?  
     drugenddateformat?  
   drugenddate?  
   druttreatmentduration?  
     druttreatmentdurationunit?  
   actiondrug?  
   drugrecurreadministration?  
   drugadditional?  
     (activesubstance*  
      drugrecurrence*  
      drugreactionrelatedness*))>  
  
<!ATTLIST drug  
  %lang.att;  
>  
  
<!ELEMENT activesubstance - -      (activesubstancename) >  
<!ATTLIST activesubstance  
  %lang.att;  
>  
  
<!ELEMENT drugrecurrence - -      (drugrecuraction) >  
<!ATTLIST drugrecurrence  
  %lang.att;  
>  
  
<!-- B.4.k.18 Relatedness of drug to reaction / event -->  
<!ELEMENT drugreactionrelatedness - -
```

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```
(drugreactionasses?
drugassessmentsource?
drugassessmentmethod?
drugresult?)>
<!ATTLIST drugreactionrelatedness
  %lang.att;
>

<!-- B.5 Narrative case summary and further information: -->
<!ELEMENT summary
  (narrativeincludeclinical?,
   reportercomment?,
   senderdiagnosis?,
   sendercomment?)>
<!ATTLIST summary
  %lang.att;
>

<!ELEMENT safetyreportid      - -      (#PCDATA) >
<!ATTLIST safetyreportid
  %lang.att;
>

<!ELEMENT safetyreportversion - -      (#PCDATA) >
<!ATTLIST safetyreportversion
  %lang.att;
>

<!-- A.1.1 Identification of the country of the primary -->
<!ELEMENT primarysourcecountry - -      (#PCDATA) >
<!ATTLIST primarysourcecountry
  %lang.att;
>

<!-- A.1.2 Identification of the country where the reaction / event occurred -->
<!ELEMENT occurcountry        - -      (#PCDATA) >
<!ATTLIST occurcountry
  %lang.att;
>

<!-- A.1.3a Date of this transmission format -->
<!ELEMENT transmissiondateformat - -      (#PCDATA) >
<!ATTLIST transmissiondateformat
  %lang.att;
>

<!-- A.1.3b Date of this transmission -->
<!ELEMENT transmissiondate      - -      (#PCDATA) >
<!ATTLIST transmissiondate
  %lang.att;
>

<!-- A.1.4 Type of report -->
<!ELEMENT reporttype          - -      (#PCDATA) >
<!ATTLIST reporttype
  %lang.att;
```

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```
>

<!-- A.1.5.1 Serious -->
<!ELEMENT serious           - -      (#PCDATA) >
<!ATTLIST serious
         %lang.att;
>

<!-- A.1.5.2 Seriousness criteria -->
<!ELEMENT seriousnessdeath   - -      (#PCDATA) >
<!ATTLIST seriousnessdeath
         %lang.att;
>
<!ELEMENT seriousnesslifethreatening - -      (#PCDATA) >
<!ATTLIST seriousnesslifethreatening
         %lang.att;
>
<!ELEMENT seriousnesshospitalization - -      (#PCDATA) >
<!ATTLIST seriousnesshospitalization
         %lang.att;
>
<!ELEMENT seriousnessdisabling   - -      (#PCDATA) >
<!ATTLIST seriousnessdisabling
         %lang.att;
>
<!ELEMENT seriousnesscongenitalanomaly - -      (#PCDATA) >
<!ATTLIST seriousnesscongenitalanomaly
         %lang.att;
>
<!ELEMENT seriousnessother     - -      (#PCDATA) >
<!ATTLIST seriousnessother
         %lang.att;
>

<!-- A.1.6a Date report was first received from source format -->
<!ELEMENT receivedateformat   - -      (#PCDATA) >
<!ATTLIST receivedateformat
         %lang.att;
>

<!-- A.1.6b Date report was first received from source -->
<!ELEMENT receivedate          - -      (#PCDATA) >
<!ATTLIST receivedate
         %lang.att;
>

<!-- A.1.7a Date of receipt of the most recent information for this report -->
<!ELEMENT receiptdateformat   - -      (#PCDATA) >
<!ATTLIST receiptdateformat
         %lang.att;
>

<!-- A.1.7b Date of receipt of the most recent information for this report -->
<!ELEMENT receiptdate          - -      (#PCDATA) >
<!ATTLIST receiptdate
         %lang.att;
>
```

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```
<!-- A.1.8.1 Are additional documents available -->
<!ELEMENT additionaldocument      - -      (#PCDATA) >
<!ATTLIST additionaldocument
      %lang.att;
>

<!-- A.1.8.2 List of documents held by sender -->
<!ELEMENT documentlist           - -      (#PCDATA) >
<!ATTLIST documentlist
      %lang.att;
>

<!-- A.1.9 Does this case fulfill the local criteria for an expedited report -->
<!ELEMENT fulfillexpeditecriteria - -      (#PCDATA) >
<!ATTLIST fulfillexpeditecriteria
      %lang.att;
>

<!--
The A.1.10 - Report Identification Numbers must be populated as per the following
user guidance:
```

A.1.10.1 and A.1.10.2 are the identifiers given by a national regulatory authority and by a company, respectively. A.1.10.3 would be used by senders who are not representing either a pharmaceutical company or a national regulatory authority. The contents of A.1.10.1, A.1.10.2, or A.1.10.3 should be populated only once, and all of these three items should remain unchanged for any transmissions subsequent to the original transmission. That is to say, these fields must only be populated once by the originator of the first transmission. Companies should ensure a single international report number (A.1.10.2) to facilitate the unique identification of a report that may have been sent to many places and subject to multiple transmissions. The contents of the fields A.1.10.1 and/or A.1.10.2 and/or A.1.10.3 should first list A.1.1 - Identification of the country of primary source and secondly list A.3.1.2 - Sender Identifier, Sender Organization, and lastly, the company international case report number, delimited by hyphens.

For example, a report transmitted by a US company to a regulatory authority would populate A.1.10.2 with "US-Company Name-12345", where "12345" is the company's unique case report number. In the event that the regulatory authority transmitted this ICSR to another regulatory authority, A.1.10.2 would remain the same. The regulatory authority would not populate A.1.10.1.

If the situation occurs where multiple reports are received about the same case, such as a report from a physician and a report from another company, the information may be merged. One number will be maintained as the case number in its original field and the second number will be listed as a suspected duplicate.

```
-->
<!-- A.1.10.1 National regulatory authority's case report number -->
<!ELEMENT authoritynumb         - -      (#PCDATA) >
<!ATTLIST authoritynumb
      %lang.att;
>

<!-- A.1.10.2 Company's case report number -->
<!ELEMENT companynumb          - -      (#PCDATA) >
<!ATTLIST companynumb
```

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```
%lang.att;
>

<!-- A.1.10.3 Other sender's case report number -->
<!ELEMENT othernumb          - -      (#PCDATA) >
<!ATTLIST othernumb
           %lang.att;
>

<!-- A.1.11 Suspected duplicate -->
<!ELEMENT duplicate          - -      (#PCDATA) >
<!ATTLIST duplicate
           %lang.att;
>

<!-- A.1.11.1 Source of the duplicate -->
<!ELEMENT duplicatesource    - -      (#PCDATA) >
<!ATTLIST duplicatesource
           %lang.att;
>

<!-- A.1.11.2 Case report number of the suspected duplicate -->
<!ELEMENT duplicatenumb     - -      (#PCDATA) >
<!ATTLIST duplicatenumb
           %lang.att;
>

<!-- A.1.12 Identification number of the report which is linked to this report -->
<!ELEMENT linkreportnumb    - -      (#PCDATA) >
<!ATTLIST linkreportnumb
           %lang.att;
>

<!-- A.1.13 Report nullification -->
<!ELEMENT casenullification - -      (#PCDATA) >
<!ATTLIST casenullification
           %lang.att;
>

<!-- A.1.13.1 Reason for nullification -->
<!ELEMENT nullificationreason - -      (#PCDATA) >
<!ATTLIST nullificationreason
           %lang.att;
>

<!-- A.1.14 Was the case medically confirmed, if not initially from health
professional? -->
<!ELEMENT medicallyconfirm   - -      (#PCDATA) >
<!ATTLIST medicallyconfirm
           %lang.att;
>

<!-- A.2.1.1a Reporter identifier -->
<!ELEMENT reportertitle     - -      (#PCDATA) >
<!ATTLIST reportertitle
           %lang.att;
>
```

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```
<!-- A.2.1.1b Reporter identifier -->
<!ELEMENT reportergivenname      - -      (#PCDATA) >
<!ATTLIST reportergivenname
      %lang.att;
>

<!-- A.2.1.1c Reporter identifier -->
<!ELEMENT reportermiddlename   - -      (#PCDATA) >
<!ATTLIST reportermiddlename
      %lang.att;
>

<!-- A.2.1.1d Reporter identifier -->
<!ELEMENT reporterfamilyname   - -      (#PCDATA) >
<!ATTLIST reporterfamilyname
      %lang.att;
>

<!-- A.2.1.2a Reporter's address -->
<!ELEMENT reporterorganization  - -      (#PCDATA) >
<!ATTLIST reporterorganization
      %lang.att;
>

<!-- A.2.1.2b Reporter's address -->
<!ELEMENT reporterdepartment    - -      (#PCDATA) >
<!ATTLIST reporterdepartment
      %lang.att;
>

<!-- A.2.1.2c Reporter's address -->
<!ELEMENT reporterstreet       - -      (#PCDATA) >
<!ATTLIST reporterstreet
      %lang.att;
>

<!-- A.2.1.2d Reporter's address -->
<!ELEMENT reportercity         - -      (#PCDATA) >
<!ATTLIST reportercity
      %lang.att;
>

<!-- A.2.1.2e Reporter's address -->
<!ELEMENT reporterstate        - -      (#PCDATA) >
<!ATTLIST reporterstate
      %lang.att;
>

<!-- A.2.1.2f Reporter's address -->
<!ELEMENT reporterpostcode     - -      (#PCDATA) >
<!ATTLIST reporterpostcode
      %lang.att;
>

<!-- A.2.1.3 Country -->
<!ELEMENT reportercountry      - -      (#PCDATA) >
```

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```
<!ATTLIST reportercountry
      %lang.att;
>

<!-- A.2.1.4 Qualification -->
<!ELEMENT qualification          - -      (#PCDATA) >
<!ATTLIST qualification
      %lang.att;
>

<!-- A.2.2 Literature reference(s) -->
<!ELEMENT literaturereference   - -      (#PCDATA) >
<!ATTLIST literaturereference
      %lang.att;
>

<!-- A.2.3.1 Study name -->
<!ELEMENT studynname           - -      (#PCDATA) >
<!ATTLIST studynname
      %lang.att;
>

<!-- A.2.3.2 Sponsor study number -->
<!ELEMENT sponsorstudynumb    - -      (#PCDATA) >
<!ATTLIST sponsorstudynumb
      %lang.att;
>

<!-- A.2.3.3 Study type in which the reactions / events were observed -->
<!ELEMENT observestudytype     - -      (#PCDATA) >
<!ATTLIST observestudytype
      %lang.att;
>

<!-- A.3.1.1 Sender type -->
<!ELEMENT sendertype           - -      (#PCDATA) >
<!ATTLIST sendertype
      %lang.att;
>

<!-- A.3.1.2 Sender organization -->
<!ELEMENT senderorganization   - -      (#PCDATA) >
<!ATTLIST senderorganization
      %lang.att;
>

<!-- A.3.1.3a Person responsible for sending the report -->
<!ELEMENT senderdepartment    - -      (#PCDATA) >
<!ATTLIST senderdepartment
      %lang.att;
>

<!-- A.3.1.3b Person responsible for sending the report -->
<!ELEMENT sendertitle         - -      (#PCDATA) >
<!ATTLIST sendertitle
      %lang.att;
>
```

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```
<!-- A.3.1.3c Person responsible for sending the report -->
<!ELEMENT sendergivenname      - -      (#PCDATA) >
<!ATTLIST sendergivenname
      %lang.att;
>

<!-- A.3.1.3d Person responsible for sending the report -->
<!ELEMENT sendermiddleinitials - -      (#PCDATA) >
<!ATTLIST sendermiddleinitials
      %lang.att;
>

<!-- A.3.1.3e Person responsible for sending the report -->
<!ELEMENT senderfamilyname     - -      (#PCDATA) >
<!ATTLIST senderfamilyname
      %lang.att;
>

<!-- A.3.1.4a Address, fax, telephone and E-mail address -->
<!ELEMENT senderstreetaddress   - -      (#PCDATA) >
<!ATTLIST senderstreetaddress
      %lang.att;
>

<!-- A.3.1.4b Address, fax, telephone and E-mail address -->
<!ELEMENT sendercity           - -      (#PCDATA) >
<!ATTLIST sendercity
      %lang.att;
>

<!-- A.3.1.4c Address, fax, telephone and E-mail address -->
<!ELEMENT senderstate          - -      (#PCDATA) >
<!ATTLIST senderstate
      %lang.att;
>

<!-- A.3.1.4d Address, fax, telephone and E-mail address -->
<!ELEMENT senderpostcode        - -      (#PCDATA) >
<!ATTLIST senderpostcode
      %lang.att;
>

<!-- A.3.1.4e Address, fax, telephone and E-mail address -->
<!ELEMENT sendercountrycode    - -      (#PCDATA) >
<!ATTLIST sendercountrycode
      %lang.att;
>

<!-- A.3.1.4f Address, fax, telephone and E-mail address -->
<!ELEMENT sendertel            - -      (#PCDATA) >
<!ATTLIST sendertel
      %lang.att;
>

<!-- A.3.1.4g Address, fax, telephone and E-mail address -->
<!ELEMENT senderteleextention  - -      (#PCDATA) >
```

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```
<!ATTLIST sendertelextension
      %lang.att;
>

<!-- A.3.1.4h Address, fax, telephone and E-mail address -->
<!ELEMENT sendertelcountrycode  - -      (#PCDATA) >
<!ATTLIST sendertelcountrycode
      %lang.att;
>

<!-- A.3.1.4i Address, fax, telephone and E-mail address -->
<!ELEMENT senderfax           - -      (#PCDATA) >
<!ATTLIST senderfax
      %lang.att;
>

<!-- A.3.1.4j Address, fax, telephone and E-mail address -->
<!ELEMENT senderfaxextension  - -      (#PCDATA) >
<!ATTLIST senderfaxextension
      %lang.att;
>

<!-- A.3.1.4k Address, fax, telephone and E-mail address -->
<!ELEMENT senderfaxcountrycode  - -      (#PCDATA) >
<!ATTLIST senderfaxcountrycode
      %lang.att;
>

<!-- A.3.1.4l Address, fax, telephone and E-mail address -->
<!ELEMENT senderemailaddress   - -      (#PCDATA) >
<!ATTLIST senderemailaddress
      %lang.att;
>

<!-- A.3.2.1 Receiver type -->
<!ELEMENT receivertype         - -      (#PCDATA) >
<!ATTLIST receivertype
      %lang.att;
>

<!-- A.3.2.2a Receiver identifier -->
<!ELEMENT receiverorganization  - -      (#PCDATA) >
<!ATTLIST receiverorganization
      %lang.att;
>

<!-- A.3.2.2b Receiver identifier -->
<!ELEMENT receiverdepartment   - -      (#PCDATA) >
<!ATTLIST receiverdepartment
      %lang.att;
>

<!-- A.3.2.2c Receiver identifier -->
<!ELEMENT receivertitle        - -      (#PCDATA) >
<!ATTLIST receivertitle
      %lang.att;
>
```

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```
<!-- A.3.2.2d Receiver identifier -->
<!ELEMENT receivergivenname      - -      (#PCDATA) >
<!ATTLIST receivergivenname
      %lang.att;
>

<!-- A.3.2.2e Receiver identifier -->
<!ELEMENT receivermiddlename   - -      (#PCDATA) >
<!ATTLIST receivermiddlename
      %lang.att;
>

<!-- A.3.2.2f Receiver identifier -->
<!ELEMENT receiverfamilyname   - -      (#PCDATA) >
<!ATTLIST receiverfamilyname
      %lang.att;
>

<!-- A.3.2.3a Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverstreetaddress - -      (#PCDATA) >
<!ATTLIST receiverstreetaddress
      %lang.att;
>

<!-- A.3.2.3b Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivercity         - -      (#PCDATA) >
<!ATTLIST receivercity
      %lang.att;
>

<!-- A.3.2.3c Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverstate        - -      (#PCDATA) >
<!ATTLIST receiverstate
      %lang.att;
>

<!-- A.3.2.3d Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverpostcode     - -      (#PCDATA) >
<!ATTLIST receiverpostcode
      %lang.att;
>

<!-- A.3.2.3e Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivercountrycode  - -      (#PCDATA) >
<!ATTLIST receivercountrycode
      %lang.att;
>

<!-- A.3.2.3f Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivertel          - -      (#PCDATA) >
<!ATTLIST receivertel
      %lang.att;
>

<!-- A.3.2.3g Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverteleextension - -      (#PCDATA) >
```

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```
<!ATTLIST receiverteleextension
      %lang.att;
>

<!-- A.3.2.3h Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receivertelcountrycode - -      (#PCDATA) >
<!ATTLIST receivertelcountrycode
      %lang.att;
>

<!-- A.3.2.3i Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverfax           - -      (#PCDATA) >
<!ATTLIST receiverfax
      %lang.att;
>

<!-- A.3.2.3j Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverfaxextension - -      (#PCDATA) >
<!ATTLIST receiverfaxextension
      %lang.att;
>

<!-- A.3.2.3k Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiverfaxcountrycode - -      (#PCDATA) >
<!ATTLIST receiverfaxcountrycode
      %lang.att;
>

<!-- A.3.2.3l Receiver's address, fax, telephone and E-mail address -->
<!ELEMENT receiveremailaddress - -      (#PCDATA) >
<!ATTLIST receiveremailaddress
      %lang.att;
>

<!-- B.1.1 Patient initials -->
<!ELEMENT patientinitial        - -      (#PCDATA) >
<!ATTLIST patientinitial
      %lang.att;
>

<!-- B.1.1.1a Patient medical record number(s) and source(s) -->
<!ELEMENT patientgpmedicalrecordnumb - -      (#PCDATA) >
<!ATTLIST patientgpmedicalrecordnumb
      %lang.att;
>

<!-- B.1.1.1b Patient medical record number(s) and source(s) -->
<!ELEMENT patientspecialistrecordnumb - -      (#PCDATA) >
<!ATTLIST patientspecialistrecordnumb
      %lang.att;
>

<!-- B.1.1.1c Patient medical record number(s) and source(s) -->
<!ELEMENT patienthospitalrecordnumb - -      (#PCDATA) >
<!ATTLIST patienthospitalrecordnumb
      %lang.att;
>
```

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```
<!-- B.1.1.1d Patient medical record number(s) and source(s) -->
<!ELEMENT patientinvestigationnumb - -      (#PCDATA) >
<!ATTLIST patientinvestigationnumb
      %lang.att;
>

<!-- B.1.2.1a Date of birth format -->
<!ELEMENT patientbirthdateformat - -      (#PCDATA) >
<!ATTLIST patientbirthdateformat
      %lang.att;
>

<!-- B.1.2.1b Date of birth -->
<!ELEMENT patientbirthdate      - -      (#PCDATA) >
<!ATTLIST patientbirthdate
      %lang.att;
>

<!-- B.1.2.2a Age at time of onset of reaction / event -->
<!ELEMENT patientonsetage      - -      (#PCDATA) >
<!ATTLIST patientonsetage
      %lang.att;
>

<!-- B.1.2.2b Age at time of onset of reaction / event unit -->
<!ELEMENT patientonsetageunit - -      (#PCDATA) >
<!ATTLIST patientonsetageunit
      %lang.att;
>

<!-- B.1.2.2.1a Gestation period when reaction / event was observed in the fetus --
>
<!ELEMENT gestationperiod      - -      (#PCDATA) >
<!ATTLIST gestationperiod
      %lang.att;
>

<!-- B.1.2.2.1b Gestation period when reaction / event was observed in the fetus
unit -->
<!ELEMENT gestationperiodunit - -      (#PCDATA) >
<!ATTLIST gestationperiodunit
      %lang.att;
>

<!-- B.1.2.3 Patient age group -->
<!ELEMENT patientagegroup      - -      (#PCDATA) >
<!ATTLIST patientagegroup
      %lang.att;
>

<!-- B.1.3 Weight (kg) -->
<!ELEMENT patientweight      - -      (#PCDATA) >
<!ATTLIST patientweight
      %lang.att;
>
```

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```
<!-- B.1.4 Height (cm) -->
<!ELEMENT patientheight          - -      (#PCDATA) >
<!ATTLIST patientheight
        %lang.att;
>

<!-- B.1.5 Sex -->
<!ELEMENT patientsex            - -      (#PCDATA) >
<!ATTLIST patientsex
        %lang.att;
>

<!-- B.1.6a Last menstrual period date format -->
<!ELEMENT lastmenstrualdateformat - -  (#PCDATA) >
<!ATTLIST lastmenstrualdateformat
        %lang.att;
>

<!-- B.1.6b Last menstrual period date -->
<!ELEMENT patientlastmenstrualdate - -  (#PCDATA) >
<!ATTLIST patientlastmenstrualdate
        %lang.att;
>

<!-- B.1.7.1a Structured information -->
<!ELEMENT patientmedicalepisodename - -  (#PCDATA) >
<!ATTLIST patientmedicalepisodename
        %lang.att;
>

<!-- B.1.7.1b Start date format -->
<!ELEMENT patientmedicalstartdateformat - -  (#PCDATA) >
<!ATTLIST patientmedicalstartdateformat
        %lang.att;
>

<!-- B.1.7.1c Start date -->
<!ELEMENT patientmedicalstartdate - -      (#PCDATA) >
<!ATTLIST patientmedicalstartdate
        %lang.att;
>

<!-- B.1.7.1d Continuing -->
<!ELEMENT patientmedicalcontinue - -      (#PCDATA) >
<!ATTLIST patientmedicalcontinue
        %lang.att;
>

<!-- B.1.7.1e End date format -->
<!ELEMENT patientmedicalenddateformat - -  (#PCDATA) >
<!ATTLIST patientmedicalenddateformat
        %lang.att;
>

<!-- B.1.7.1f End date -->
<!ELEMENT patientmedicalenddate - -      (#PCDATA) >
<!ATTLIST patientmedicalenddate
```

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```
%lang.att;
>

<!-- B.1.7.1g Comments -->
<!ELEMENT patientmedicalcomment - -      (#PCDATA) >
<!ATTLIST patientmedicalcomment
      %lang.att;
>

<!-- B.1.7.2 Text for relevant medical history and concurrent conditions -->
<!ELEMENT patientmedicalhistorytext - - (#PCDATA) >
<!ATTLIST patientmedicalhistorytext
      %lang.att;
>

<!-- B.1.8a Name of drug -->
<!ELEMENT patientdrugname      - -      (#PCDATA) >
<!ATTLIST patientdrugname
      %lang.att;
>

<!-- B.1.8b Start date format -->
<!ELEMENT patientdrugstartdateformat - - (#PCDATA) >
<!ATTLIST patientdrugstartdateformat
      %lang.att;
>

<!-- B.1.8c Start date -->
<!ELEMENT patientdrugstartdate      - -      (#PCDATA) >
<!ATTLIST patientdrugstartdate
      %lang.att;
>

<!-- B.1.8d End date format -->
<!ELEMENT patientdrugenddateformat - -      (#PCDATA) >
<!ATTLIST patientdrugenddateformat
      %lang.att;
>

<!-- B.1.8e End date -->
<!ELEMENT patientdrugenddate      - -      (#PCDATA) >
<!ATTLIST patientdrugenddate
      %lang.att;
>

<!-- B.1.8f Indication -->
<!ELEMENT patientdrugindication - -      (#PCDATA) >
<!ATTLIST patientdrugindication
      %lang.att;
>

<!-- B.1.8g Reaction -->
<!ELEMENT patientdrugreaction     - -      (#PCDATA) >
<!ATTLIST patientdrugreaction
      %lang.att;
>

<!-- B.1.9.1a Date of death format -->
```

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```
<!ELEMENT patientdeathdateformat - -      (#PCDATA) >
<!ATTLIST patientdeathdateformat
      %lang.att;
>

<!-- B.1.9.1b Date of death --&gt;
&lt;!ELEMENT patientdeathdate      - -      (#PCDATA) &gt;
&lt;!ATTLIST patientdeathdate
      %lang.att;
&gt;

<!-- B.1.9.2 Reported cause of death --&gt;
&lt;!ELEMENT patientdeathreport    - -      (#PCDATA) &gt;
&lt;!ATTLIST patientdeathreport
      %lang.att;
&gt;

<!-- B.1.9.3 Was autopsy done? --&gt;
&lt;!ELEMENT patientautopsyyesno   - -      (#PCDATA) &gt;
&lt;!ATTLIST patientautopsyyesno
      %lang.att;
&gt;

<!-- B.1.9.4 Autopsy-determined causes(s) of death --&gt;
&lt;!ELEMENT patientdetermineautopsy - -      (#PCDATA) &gt;
&lt;!ATTLIST patientdetermineautopsy
      %lang.att;
&gt;

<!-- B.1.10.1 Parent identification --&gt;
&lt;!ELEMENT parentidentification   - -      (#PCDATA) &gt;
&lt;!ATTLIST parentidentification
      %lang.att;
&gt;

<!-- B.1.10.2.1a Date of birth of parent format --&gt;
&lt;!ELEMENT parentbirthdateformat - -      (#PCDATA) &gt;
&lt;!ATTLIST parentbirthdateformat
      %lang.att;
&gt;

<!-- B.1.10.2.1b Date of birth of parent --&gt;
&lt;!ELEMENT parentbirthdate      - -      (#PCDATA) &gt;
&lt;!ATTLIST parentbirthdate
      %lang.att;
&gt;

<!-- B.1.10.2.2a Age of parent --&gt;
&lt;!ELEMENT parentage            - -      (#PCDATA) &gt;
&lt;!ATTLIST parentage
      %lang.att;
&gt;

<!-- B.1.10.2.2b Age of parent unit --&gt;
&lt;!ELEMENT parentageunit        - -      (#PCDATA) &gt;
&lt;!ATTLIST parentageunit
      %lang.att;</pre>
```

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```
>

<!-- B.1.10.3a Last menstrual period format -->
<!ELEMENT parentlastmenstrualdateformat - -      (#PCDATA) >
<!ATTLIST parentlastmenstrualdateformat
      %lang.att;
>

<!-- B.1.10.3b Last menstrual period -->
<!ELEMENT parentlastmenstrualdate - -      (#PCDATA) >
<!ATTLIST parentlastmenstrualdate
      %lang.att;
>

<!-- B.1.10.4 Weight (kg) of parent -->
<!ELEMENT parentweight          - -      (#PCDATA) >
<!ATTLIST parentweight
      %lang.att;
>

<!-- B.1.10.5 Height (cm) of parent -->
<!ELEMENT parentheight         - -      (#PCDATA) >
<!ATTLIST parentheight
      %lang.att;
>

<!-- B.1.10.6 Sex of parent -->
<!ELEMENT parentsex            - -      (#PCDATA) >
<!ATTLIST parentsex
      %lang.att;
>

<!-- B.1.10.7.1a Structured information -->
<!ELEMENT parentmedicalepisodename - -      (#PCDATA) >
<!ATTLIST parentmedicalepisodename
      %lang.att;
>

<!-- B.1.10.7.1b Start date format -->
<!ELEMENT parentmedicalstartdateformat - -      (#PCDATA) >
<!ATTLIST parentmedicalstartdateformat
      %lang.att;
>

<!-- B.1.10.7.1c Start date -->
<!ELEMENT parentmedicalstartdate - -      (#PCDATA) >
<!ATTLIST parentmedicalstartdate
      %lang.att;
>

<!-- B.1.10.7.1d Continuing -->
<!ELEMENT parentmedicalcontinue - -      (#PCDATA) >
<!ATTLIST parentmedicalcontinue
      %lang.att;
>

<!-- B.1.10.7.1e End date format -->
<!ELEMENT parentmedicalenddateformat - -      (#PCDATA) >
<!ATTLIST parentmedicalenddateformat
```

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```
%lang.att;
>

<!-- B.1.10.7.1f End date -->
<!ELEMENT parentmedicalenddate - -      (#PCDATA) >
<!ATTLIST parentmedicalenddate
      %lang.att;
>

<!-- B.1.10.7.1g Comments -->
<!ELEMENT parentmedicalcomment - -      (#PCDATA) >
<!ATTLIST parentmedicalcomment
      %lang.att;
>

<!-- B.1.10.7.2 Text for relevant medical history and concurrent conditions (not
including reaction / event) of parent -->
<!ELEMENT parentmedicalrelevanttext - -      (#PCDATA) >
<!ATTLIST parentmedicalrelevanttext
      %lang.att;
>

<!-- B.1.10.8a Name of drug as -->
<!ELEMENT parentdrugname      - -      (#PCDATA) >
<!ATTLIST parentdrugname
      %lang.att;
>

<!-- B.1.10.8b Start date format -->
<!ELEMENT parentdrugstartdateformat - -      (#PCDATA) >
<!ATTLIST parentdrugstartdateformat
      %lang.att;
>

<!-- B.1.10.8c Start date -->
<!ELEMENT parentdrugstartdate      - -      (#PCDATA) >
<!ATTLIST parentdrugstartdate
      %lang.att;
>

<!-- B.1.10.8d End date format -->
<!ELEMENT parentdrugenddateformat - -      (#PCDATA) >
<!ATTLIST parentdrugenddateformat
      %lang.att;
>

<!-- B.1.10.8e End date -->
<!ELEMENT parentdrugenddate      - -      (#PCDATA) >
<!ATTLIST parentdrugenddate
      %lang.att;
>

<!-- B.1.10.8f Indication -->
<!ELEMENT parentdrugindication - -      (#PCDATA) >
<!ATTLIST parentdrugindication
      %lang.att;
>
```

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```
<!-- B.1.10.8g Reactions (if any and known) -->
<!ELEMENT parentdrugreaction      - -      (#PCDATA) >
<!ATTLIST parentdrugreaction
      %lang.att;
>

<!-- B.2.i.1 Reaction / event as reported by primary -->
<!ELEMENT primarysourcereaction - -      (#PCDATA) >
<!ATTLIST primarysourcereaction
      %lang.att;
>

<!-- B.2.i.2 Reaction / event term -->
<!ELEMENT reactionterm          - -      (#PCDATA) >
<!ATTLIST reactionterm
      %lang.att;
>

<!-- B.2.i.3 Term highlighted by the reporter -->
<!ELEMENT termhighlighted      - -      (#PCDATA) >
<!ATTLIST termhighlighted
      %lang.att;
>

<!-- B.2.i.4a Date of start of reaction / event format -->
<!ELEMENT reactionstartdateformat - -      (#PCDATA) >
<!ATTLIST reactionstartdateformat
      %lang.att;
>

<!-- B.2.i.4b Date of start of reaction / event -->
<!ELEMENT reactionstartdate     - -      (#PCDATA) >
<!ATTLIST reactionstartdate
      %lang.att;
>

<!-- B.2.i.5a Date of end of reaction / event format -->
<!ELEMENT reactionenddateformat - -      (#PCDATA) >
<!ATTLIST reactionenddateformat
      %lang.att;
>

<!-- B.2.i.5b Date of end of reaction / event -->
<!ELEMENT reactionenddate       - -      (#PCDATA) >
<!ATTLIST reactionenddate
      %lang.att;
>

<!-- B.2.i.6a Duration of reaction / event -->
<!ELEMENT reactionduration      - -      (#PCDATA) >
<!ATTLIST reactionduration
      %lang.att;
>

<!-- B.2.i.6b Duration of reaction / event unit -->
<!ELEMENT reactiondurationunit - -      (#PCDATA) >
<!ATTLIST reactiondurationunit
      %lang.att;
```

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```
>

<!-- B.2.i.7.1a Time interval between beginning of suspect drug administration and
start of reaction / event -->
<!ELEMENT reactionfirsttime      - -      (#PCDATA) >
<!ATTLIST reactionfirsttime
      %lang.att;
>

<!-- B.2.i.7.1b Time interval between beginning of suspect drug administration and
start of reaction / event unit -->
<!ELEMENT reactionfirsttimeunit - -      (#PCDATA) >
<!ATTLIST reactionfirsttimeunit
      %lang.att;
>

<!-- B.2.i.7.2a Time interval between last dose and start of reaction / event -->
<!ELEMENT reactionlasttime      - -      (#PCDATA) >
<!ATTLIST reactionlasttime
      %lang.att;
>

<!-- B.2.i.7.2b Time interval between last dose and start of reaction / event unit
-->
<!ELEMENT reactionlasttimeunit - -      (#PCDATA) >
<!ATTLIST reactionlasttimeunit
      %lang.att;
>

<!-- B.2.i.8 Outcome of reaction / event at the time of last observation -->
<!ELEMENT reactionoutcome      - -      (#PCDATA) >
<!ATTLIST reactionoutcome
      %lang.att;
>

<!-- B.3.1a Date format -->
<!ELEMENT testdateformat      - -      (#PCDATA) >
<!ATTLIST testdateformat
      %lang.att;
>

<!-- B.3.1b Date -->
<!ELEMENT testdate      - -      (#PCDATA) >
<!ATTLIST testdate
      %lang.att;
>

<!-- B.3.1c Test -->
<!ELEMENT testname      - -      (#PCDATA) >
<!ATTLIST testname
      %lang.att;
>

<!-- B.3.1d Result -->
<!ELEMENT testresult      - -      (#PCDATA) >
<!ATTLIST testresult
      %lang.att;
```

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```
>

<!-- B.3.1e Unit -->
<!ELEMENT testunit          - -      (#PCDATA) >
<!ATTLIST testunit
      %lang.att;
>

<!-- B.3.1.1 Normal low range -->
<!ELEMENT lowtestrange     - -      (#PCDATA) >
<!ATTLIST lowtestrange
      %lang.att;
>

<!-- B.3.1.2 Normal high range -->
<!ELEMENT hightestrange    - -      (#PCDATA) >
<!ATTLIST hightestrange
      %lang.att;
>

<!-- B.3.1.3 More information available (Y/N) -->
<!ELEMENT moreinformation   - -      (#PCDATA) >
<!ATTLIST moreinformation
      %lang.att;
>

<!-- B.3.2 Results of tests and procedures relevant to the investigation of the
patient -->
<!ELEMENT resultstestsprocedures - -      (#PCDATA) >
<!ATTLIST resultstestsprocedures
      %lang.att;
>

<!-- B.4.k.1 Characterization of drug -->
<!ELEMENT drugcharacterization - -      (#PCDATA) >
<!ATTLIST drugcharacterization
      %lang.att;
>

<!-- B.4.k.2.1 Proprietary medicinal product name -->
<!ELEMENT medicinalproduct   - -      (#PCDATA) >
<!ATTLIST medicinalproduct
      %lang.att;
>

<!-- B.4.k.2.2 Active drug substance names -->
<!ELEMENT activesubstancename - -      (#PCDATA) >
<!ATTLIST activesubstancename
      %lang.att;
>

<!-- B.4.k.2.2 Identification of the country where the drug was obtained -->
<!ELEMENT obtaindrugcountry  - -      (#PCDATA) >
<!ATTLIST obtaindrugcountry
      %lang.att;
>
```

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```
<!-- B.4.k.3 Batch / lot number -->
<!ELEMENT drugbatchnumb - - (#PCDATA) >
<!ATTLIST drugbatchnumb
      %lang.att;
>

<!-- B.4.k.4.1 Authorization / application number -->
<!ELEMENT drugauthorizationnumb - - (#PCDATA) >
<!ATTLIST drugauthorizationnumb
      %lang.att;
>

<!-- B.4.k.4.2 Country of authorization / application -->
<!ELEMENT drugauthorizationcountry - - (#PCDATA) >
<!ATTLIST drugauthorizationcountry
      %lang.att;
>

<!-- B.4.k.4.3 Name of holder/applicant -->
<!ELEMENT drugauthorizationholder - - (#PCDATA) >
<!ATTLIST drugauthorizationholder
      %lang.att;
>

<!-- B.4.k.5.1 Dose (number) -->
<!ELEMENT drugstructuredosagenumb - - (#PCDATA) >
<!ATTLIST drugstructuredosagenumb
      %lang.att;
>

<!-- B.4.k.5.2 Dose (unit) -->
<!ELEMENT drugstructuredosageunit - - (#PCDATA) >
<!ATTLIST drugstructuredosageunit
      %lang.att;
>

<!-- B.4.k.5.3 Number of separate -->
<!ELEMENT drugseparatedosagenumb - - (#PCDATA) >
<!ATTLIST drugseparatedosagenumb
      %lang.att;
>

<!-- B.4.k.5.4 Number of units in the interval -->
<!ELEMENT drugintervaldosageunitnumb - - (#PCDATA) >
<!ATTLIST drugintervaldosageunitnumb
      %lang.att;
>

<!-- B.4.k.5.5 Definition of the interval -->
<!ELEMENT drugintervaldosagedefinition - - (#PCDATA) >
<!ATTLIST drugintervaldosagedefinition
      %lang.att;
>

<!-- B.4.k.5.6 Cumulative dose to first reaction (number) -->
<!ELEMENT drugcumulativedosagenumb - - (#PCDATA) >
<!ATTLIST drugcumulativedosagenumb
```

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```
%lang.att;
>

<!-- B.4.k.5.7 Cumulative dose to first reaction (unit) -->
<!ELEMENT drugcumulativedosageunit - - (#PCDATA) >
<!ATTLIST drugcumulativedosageunit
      %lang.att;
>

<!-- B.4.k.6 Dosage text -->
<!ELEMENT drugdosagetext      - -      (#PCDATA) >
<!ATTLIST drugdosagetext
      %lang.att;
>

<!-- B.4.k.7 Pharmaceutical form (Dosage form) -->
<!ELEMENT drugdosageform      - -      (#PCDATA) >
<!ATTLIST drugdosageform
      %lang.att;
>

<!-- B.4.k.8 Route of administration -->
<!ELEMENT drugadministrationroute - - (#PCDATA) >
<!ATTLIST drugadministrationroute
      %lang.att;
>

<!-- B.4.k.9 Parent route of administration (in case of a parent child / fetus report) -->
<!ELEMENT drugparadministration - - (#PCDATA) >
<!ATTLIST drugparadministration
      %lang.att;
>

<!-- B.4.k.10a Gestation period at time of exposure -->
<!ELEMENT reactiongestationperiod - - (#PCDATA) >
<!ATTLIST reactiongestationperiod
      %lang.att;
>

<!-- B.4.k.10b Gestation period at time of exposure unit -->
<!ELEMENT reactiongestationperiodunit    - -      (#PCDATA) >
<!ATTLIST reactiongestationperiodunit
      %lang.att;
>

<!-- B.4.k.11 Indication for use in the case -->
<!ELEMENT drugindication      - -      (#PCDATA) >
<!ATTLIST drugindication
      %lang.att;
>

<!-- B.4.k.12a Date of start of drug format -->
<!ELEMENT drugstartdateformat    - -      (#PCDATA) >
<!ATTLIST drugstartdateformat
      %lang.att;
```

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```
>

<!-- B.4.k.12b Date of start of drug -->
<!ELEMENT drugstartdate      - -      (#PCDATA) >
<!ATTLIST drugstartdate
      %lang.att;
>

<!-- B.4.k.13.1a Time interval between beginning of drug administration and start
of reaction / event -->
<!ELEMENT drugstartperiod    - -      (#PCDATA) >
<!ATTLIST drugstartperiod
      %lang.att;
>

<!-- B.4.k.13.1b Time interval between beginning of drug administration and start
of reaction / event unit -->
<!ELEMENT drugstartperiodunit - -      (#PCDATA) >
<!ATTLIST drugstartperiodunit
      %lang.att;
>

<!-- fB.4.k.13.2a Time interval between last dose of drug and start of reaction /
event -->
<!ELEMENT druglastperiod     - -      (#PCDATA) >
<!ATTLIST druglastperiod
      %lang.att;
>

<!-- B.4.k.13.2b Time interval between last dose of drug and start of reaction /
event unit -->
<!ELEMENT druglastperiodunit - -      (#PCDATA) >
<!ATTLIST druglastperiodunit
      %lang.att;
>

<!-- B.4.k.14a Date of last administration format -->
<!ELEMENT drugenddateformat - -      (#PCDATA) >
<!ATTLIST drugenddateformat
      %lang.att;
>

<!-- B.4.k.14b Date of last administration -->
<!ELEMENT drugenddate        - -      (#PCDATA) >
<!ATTLIST drugenddate
      %lang.att;
>

<!-- B.4.k.15a Duration of drug administration unit -->
<!ELEMENT drughtreatmentduration - -      (#PCDATA) >
<!ATTLIST drughtreatmentduration
      %lang.att;
>

<!-- B.4.k.15b Duration of drug administration unit -->
<!ELEMENT drughtreatmentdurationunit - -      (#PCDATA) >
<!ATTLIST drughtreatmentdurationunit
```

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```
%lang.att;
>

<!-- B.4.k.16 Action(s) taken with drug -->
<!ELEMENT actiondrug          - -      (#PCDATA) >
<!ATTLIST actiondrug
      %lang.att;
>

<!-- B.4.k.17.1 Did reaction recur on readministration? -->
<!ELEMENT drugrecurreadministration - - (#PCDATA) >
<!ATTLIST drugrecurreadministration
      %lang.att;
>

<!-- B.4.k.17.2 If yes, which reaction / event recurred? -->
<!ELEMENT drugrecuraction      - -      (#PCDATA) >
<!ATTLIST drugrecuraction
      %lang.att;
>

<!-- B.4.k.18.1 Reaction assessed -->
<!ELEMENT drugreactionasses   - -      (#PCDATA) >
<!ATTLIST drugreactionasses
      %lang.att;
>

<!-- B.4.k.18.2 Source of assessment -->
<!ELEMENT drugassessmentsource - -      (#PCDATA) >
<!ATTLIST drugassessmentsource
      %lang.att;
>

<!-- B.4.k.18.3 Method of assessment -->
<!ELEMENT drugassessmentmethod - -      (#PCDATA) >
<!ATTLIST drugassessmentmethod
      %lang.att;
>

<!-- B.4.k.18.4 Result -->
<!ELEMENT drugresult           - -      (#PCDATA) >
<!ATTLIST drugresult
      %lang.att;
>

<!-- B.4.k.19 Additional information on drug -->
<!ELEMENT drugadditional       - -      (#PCDATA) >
<!ATTLIST drugadditional
      %lang.att;
>

<!-- B.5.1 Case narrative including clinical course, therapeutic measures, outcome
and additional relevant information -->
<!ELEMENT narrativeincludeclinical - - (#PCDATA) >
<!ATTLIST narrativeincludeclinical
      %lang.att;
>
```

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```
<!-- B.5.2 Reporter's comments -->
<!ELEMENT reportercomment      - -      (#PCDATA) >
<!ATTLIST reportercomment
  %lang.att;
>

<!-- B.5.3 Sender's diagnosis / syndrome and / or reclassification of reaction /
event -->
<!ELEMENT senderdiagnosis     - -      (#PCDATA) >
<!ATTLIST senderdiagnosis
  %lang.att;
>

<!-- B.5.4 Sender's comments -->
<!ELEMENT sendercomment       - -      (#PCDATA) >
<!ATTLIST sendercomment
  %lang.att;
>
] >
```

### A.3 Declaration (DCL) Files for Multi-Language Character Sets

Five SGML declarations are included with the ICH ICSR distribution.

**ichicsr-latin1.dcl** - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

```
<!SGML "ISO 8879:1986"
--
   SGML Declaration for ICHICSR SGML Applications using ISO Latin 1.
   This Declaration is a virtual copy of the SGML Declaration
   for HyperText Markup Language version 3.2.

   With support for ISO Latin-1 and increased limits
   for tag and literal lengths etc.
--

CHARSET
  BASESET "ISO 646:1983//CHARSET
            International Reference Version
            (IRV)//ESC 2/5 4/0"
  DESCSET 0   9   UNUSED
          9   2   9
          11  2   UNUSED
          13  1   13
          14  18  UNUSED
          32  95  32
          127 1   UNUSED
  BASESET "ISO Registration Number 100//CHARSET
            ECMA-94 Right Part of
            Latin Alphabet Nr. 1//ESC 2/13 4/1"
  DESCSET 128 32  UNUSED
          160 96   32

CAPACITY  SGMLREF
  TOTALCAP      200000
  GRPCAP        150000
  ENTCAP        150000

SCOPE     DOCUMENT
SYNTAX
  SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
               17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
  BASESET "ISO 646:1983//CHARSET
            International Reference Version
            (IRV)//ESC 2/5 4/0"
  DESCSET 0 128 0

FUNCTION
  RE           13
  RS           10
  SPACE        32
  TAB SEPCHAR  9

NAMING    LCNMSTRT ""
```

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```
UCNMSTRT ""
LCNMCHAR ". - "
UCNMCHAR ". - "
NAMECASE GENERAL YES
ENTITY NO
DELIM GENERAL SGMLREF
SHORTREF SGMLREF
NAMES SGMLREF
QUANTITY SGMLREF
ATTSPLEN 65536
LITLEN 65536
NAMELEN 32
PILEN 65536
TAGLVL 100
TAGLEN 65536
GRPGTCNT 150
GRPCNT 64

FEATURES
MINIMIZE
DATATAG NO
OMITTAG NO
RANK NO
SHORTTAG YES
LINK
SIMPLE NO
IMPLICIT NO
EXPLICIT NO
OTHER
CONCUR NO
SUBDOC NO
FORMAL YES
APPINFO NONE
>
```

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**ichicsr-latin7.dcl** - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

```
<!SGML "ISO 8879:1986"
--
    SGML Declaration for ICHICSR SGML Applications using ISO Latin 7.
    This Declaration is a virtual copy of the SGML Declaration
    for HyperText Markup Language version 3.2.

    With support for ISO Latin-7 and increased limits
        for tag and literal lengths etc.

--
CHARSET
BASESET "ISO 646:1983//CHARSET
          International Reference Version
          (IRV)//ESC 2/5 4/0"
DESCSET 0   9   UNUSED
         9   2   9
         11  2   UNUSED
         13  1   13
         14  18  UNUSED
         32  95  32
         127 1   UNUSED
BASESET "ISO Registration Number 100//CHARSET
          ECMA-94 Right Part of
          Latin Alphabet Nr. 1//ESC 2/13 4/7"
DESCSET 128 32  UNUSED
         160 96   32

CAPACITY SGMLREF
TOTALCAP      200000
GRPCAP       150000
ENTCAP       150000

SCOPE DOCUMENT
SYNTAX
SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
                  17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127
BASESET "ISO 646:1983//CHARSET
          International Reference Version
          (IRV)//ESC 2/5 4/0"
DESCSET 0 128 0

FUNCTION
RE           13
RS           10
SPACE        32
TAB SEPCHAR  9

NAMING LCNMSTRT ""
UCNMSTRT ""
LCNMCHAR ".-"
UCNMCHAR ".-"
NAMECASE GENERAL YES
ENTITY      NO
```

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DELIM GENERAL SGMLREF  
          SHORTREF SGMLREF  
NAMES SGMLREF  
QUANTITY SGMLREF  
          ATTRSLEN 65536  
          LITLEN 65536  
          NAMELEN 32  
          PILEN 65536  
          TAGLVL 100  
          TAGLEN 65536  
          GRPGTCNT 150  
          GRPCNT 64

FEATURES  
MINIMIZE  
  DATATAG NO  
  OMITTAG NO  
  RANK NO  
  SHORTTAG YES  
LINK  
  SIMPLE NO  
  IMPLICIT NO  
  EXPLICIT NO  
OTHER  
  CONCUR NO  
  SUBDOC NO  
  FORMAL YES  
APPINFO NONE

>

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**ichicsr-sjis.dcl** – This SGML declaration supports the Shift JIS character set for encoding Japanese.

```
<! SGML "ISO 8879:1986"
-- 
SGML Declaration for ICH SGML Applications using sjis.
This Declaration was written by James Clark for
the SP parser.

This character set declaration is suitable for use with the ujis or
sjis coding systems. It's probably rather easier to lie a bit.
--

CHARSET
BASESET
"ISO Registration Number 1//CHARSET C0 set of ISO 646//ESC 2/1 4/0"
DESCSET      0      9      UNUSED
            9      2      9
            11     2      UNUSED
            13     1      13
            14    18      UNUSED

BASESET
"ISO Registration Number 14//CHARSET ISO 646 Japanese Version//ESC 2/8 4/10"
DESCSET
32 95 32
127 1 UNUSED

BASESET
"ISO Registration Number 87//CHARSET JIS X 0208-1990//ESC 2/6 4/0 ESC 2/4
4/2"

DESCSET
41344 33 UNUSED
41377 94 8481
41471 1 UNUSED
41600 33 UNUSED
41633 94 8737
41727 1 UNUSED
41856 33 UNUSED
41889 94 8993
41983 1 UNUSED
42112 33 UNUSED
42145 94 9249
42239 1 UNUSED
42368 33 UNUSED
42401 94 9505
42495 1 UNUSED
42624 33 UNUSED
42657 94 9761
42751 1 UNUSED
42880 33 UNUSED
42913 94 10017
43007 1 UNUSED
43136 33 UNUSED
43169 94 10273
43263 1 UNUSED
```

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43392 33 UNUSED  
43425 94 10529  
43519 1 UNUSED  
43648 33 UNUSED  
43681 94 10785  
43775 1 UNUSED  
43904 33 UNUSED  
43937 94 11041  
44031 1 UNUSED  
44160 33 UNUSED  
44193 94 11297  
44287 1 UNUSED  
44416 33 UNUSED  
44449 94 11553  
44543 1 UNUSED  
44672 33 UNUSED  
44705 94 11809  
44799 1 UNUSED  
44928 33 UNUSED  
44961 94 12065  
45055 1 UNUSED  
45184 33 UNUSED  
45217 94 12321  
45311 1 UNUSED  
45440 33 UNUSED  
45473 94 12577  
45567 1 UNUSED  
45696 33 UNUSED  
45729 94 12833  
45823 1 UNUSED  
45952 33 UNUSED  
45985 94 13089  
46079 1 UNUSED  
46208 33 UNUSED  
46241 94 13345  
46335 1 UNUSED  
46464 33 UNUSED  
46497 94 13601  
46591 1 UNUSED  
46720 33 UNUSED  
46753 94 13857  
46847 1 UNUSED  
46976 33 UNUSED  
47009 94 14113  
47103 1 UNUSED  
47232 33 UNUSED  
47265 94 14369  
47359 1 UNUSED  
47488 33 UNUSED  
47521 94 14625  
47615 1 UNUSED  
47744 33 UNUSED  
47777 94 14881  
47871 1 UNUSED  
48000 33 UNUSED  
48033 94 15137  
48127 1 UNUSED

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48256 33 UNUSED  
48289 94 15393  
48383 1 UNUSED  
48512 33 UNUSED  
48545 94 15649  
48639 1 UNUSED  
48768 33 UNUSED  
48801 94 15905  
48895 1 UNUSED  
49024 33 UNUSED  
49057 94 16161  
49151 1 UNUSED  
49280 33 UNUSED  
49313 94 16417  
49407 1 UNUSED  
49536 33 UNUSED  
49569 94 16673  
49663 1 UNUSED  
49792 33 UNUSED  
49825 94 16929  
49919 1 UNUSED  
50048 33 UNUSED  
50081 94 17185  
50175 1 UNUSED  
50304 33 UNUSED  
50337 94 17441  
50431 1 UNUSED  
50560 33 UNUSED  
50593 94 17697  
50687 1 UNUSED  
50816 33 UNUSED  
50849 94 17953  
50943 1 UNUSED  
51072 33 UNUSED  
51105 94 18209  
51199 1 UNUSED  
51328 33 UNUSED  
51361 94 18465  
51455 1 UNUSED  
51584 33 UNUSED  
51617 94 18721  
51711 1 UNUSED  
51840 33 UNUSED  
51873 94 18977  
51967 1 UNUSED  
52096 33 UNUSED  
52129 94 19233  
52223 1 UNUSED  
52352 33 UNUSED  
52385 94 19489  
52479 1 UNUSED  
52608 33 UNUSED  
52641 94 19745  
52735 1 UNUSED  
52864 33 UNUSED  
52897 94 20001  
52991 1 UNUSED

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53120 33 UNUSED  
53153 94 20257  
53247 1 UNUSED  
53376 33 UNUSED  
53409 94 20513  
53503 1 UNUSED  
53632 33 UNUSED  
53665 94 20769  
53759 1 UNUSED  
53888 33 UNUSED  
53921 94 21025  
54015 1 UNUSED  
54144 33 UNUSED  
54177 94 21281  
54271 1 UNUSED  
54400 33 UNUSED  
54433 94 21537  
54527 1 UNUSED  
54656 33 UNUSED  
54689 94 21793  
54783 1 UNUSED  
54912 33 UNUSED  
54945 94 22049  
55039 1 UNUSED  
55168 33 UNUSED  
55201 94 22305  
55295 1 UNUSED  
55424 33 UNUSED  
55457 94 22561  
55551 1 UNUSED  
55680 33 UNUSED  
55713 94 22817  
55807 1 UNUSED  
55936 33 UNUSED  
55969 94 23073  
56063 1 UNUSED  
56192 33 UNUSED  
56225 94 23329  
56319 1 UNUSED  
56448 33 UNUSED  
56481 94 23585  
56575 1 UNUSED  
56704 33 UNUSED  
56737 94 23841  
56831 1 UNUSED  
56960 33 UNUSED  
56993 94 24097  
57087 1 UNUSED  
57216 33 UNUSED  
57249 94 24353  
57343 1 UNUSED  
57472 33 UNUSED  
57505 94 24609  
57599 1 UNUSED  
57728 33 UNUSED  
57761 94 24865  
57855 1 UNUSED

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57984 33 UNUSED  
58017 94 25121  
58111 1 UNUSED  
58240 33 UNUSED  
58273 94 25377  
58367 1 UNUSED  
58496 33 UNUSED  
58529 94 25633  
58623 1 UNUSED  
58752 33 UNUSED  
58785 94 25889  
58879 1 UNUSED  
59008 33 UNUSED  
59041 94 26145  
59135 1 UNUSED  
59264 33 UNUSED  
59297 94 26401  
59391 1 UNUSED  
59520 33 UNUSED  
59553 94 26657  
59647 1 UNUSED  
59776 33 UNUSED  
59809 94 26913  
59903 1 UNUSED  
60032 33 UNUSED  
60065 94 27169  
60159 1 UNUSED  
60288 33 UNUSED  
60321 94 27425  
60415 1 UNUSED  
60544 33 UNUSED  
60577 94 27681  
60671 1 UNUSED  
60800 33 UNUSED  
60833 94 27937  
60927 1 UNUSED  
61056 33 UNUSED  
61089 94 28193  
61183 1 UNUSED  
61312 33 UNUSED  
61345 94 28449  
61439 1 UNUSED  
61568 33 UNUSED  
61601 94 28705  
61695 1 UNUSED  
61824 33 UNUSED  
61857 94 28961  
61951 1 UNUSED  
62080 33 UNUSED  
62113 94 29217  
62207 1 UNUSED  
62336 33 UNUSED  
62369 94 29473  
62463 1 UNUSED  
62592 33 UNUSED  
62625 94 29729  
62719 1 UNUSED

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62848 33 UNUSED  
62881 94 29985  
62975 1 UNUSED  
63104 33 UNUSED  
63137 94 30241  
63231 1 UNUSED  
63360 33 UNUSED  
63393 94 30497  
63487 1 UNUSED  
63616 33 UNUSED  
63649 94 30753  
63743 1 UNUSED  
63872 33 UNUSED  
63905 94 31009  
63999 1 UNUSED  
64128 33 UNUSED  
64161 94 31265  
64255 1 UNUSED  
64384 33 UNUSED  
64417 94 31521  
64511 1 UNUSED  
64640 33 UNUSED  
64673 94 31777  
64767 1 UNUSED  
64896 33 UNUSED  
64929 94 32033  
65023 1 UNUSED  
65152 33 UNUSED  
65185 94 32289  
65279 1 UNUSED

BASESET

"ISO Registration Number 13//CHARSET JIS X 0201-1986//ESC 2/8 4/9"  
-- JIS C 6220-1969 --

DESCSET

128 33 UNUSED  
161 94 33  
255 1 UNUSED  
256 40960 UNUSED

BASESET

"ISO Registration Number 159//CHARSET JIS X 0212-1990//ESC 2/4 2/8 4/4"

DESCSET

41216 33 UNUSED  
41249 94 8481  
41343 1 UNUSED  
41472 33 UNUSED  
41505 94 8737  
41599 1 UNUSED  
41728 33 UNUSED  
41761 94 8993  
41855 1 UNUSED  
41984 33 UNUSED  
42017 94 9249  
42111 1 UNUSED  
42240 33 UNUSED

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42273 94 9505  
42367 1 UNUSED  
42496 33 UNUSED  
42529 94 9761  
42623 1 UNUSED  
42752 33 UNUSED  
42785 94 10017  
42879 1 UNUSED  
43008 33 UNUSED  
43041 94 10273  
43135 1 UNUSED  
43264 33 UNUSED  
43297 94 10529  
43391 1 UNUSED  
43520 33 UNUSED  
43553 94 10785  
43647 1 UNUSED  
43776 33 UNUSED  
43809 94 11041  
43903 1 UNUSED  
44032 33 UNUSED  
44065 94 11297  
44159 1 UNUSED  
44288 33 UNUSED  
44321 94 11553  
44415 1 UNUSED  
44544 33 UNUSED  
44577 94 11809  
44671 1 UNUSED  
44800 33 UNUSED  
44833 94 12065  
44927 1 UNUSED  
45056 33 UNUSED  
45089 94 12321  
45183 1 UNUSED  
45312 33 UNUSED  
45345 94 12577  
45439 1 UNUSED  
45568 33 UNUSED  
45601 94 12833  
45695 1 UNUSED  
45824 33 UNUSED  
45857 94 13089  
45951 1 UNUSED  
46080 33 UNUSED  
46113 94 13345  
46207 1 UNUSED  
46336 33 UNUSED  
46369 94 13601  
46463 1 UNUSED  
46592 33 UNUSED  
46625 94 13857  
46719 1 UNUSED  
46848 33 UNUSED  
46881 94 14113  
46975 1 UNUSED  
47104 33 UNUSED

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47137 94 14369  
47231 1 UNUSED  
47360 33 UNUSED  
47393 94 14625  
47487 1 UNUSED  
47616 33 UNUSED  
47649 94 14881  
47743 1 UNUSED  
47872 33 UNUSED  
47905 94 15137  
47999 1 UNUSED  
48128 33 UNUSED  
48161 94 15393  
48255 1 UNUSED  
48384 33 UNUSED  
48417 94 15649  
48511 1 UNUSED  
48640 33 UNUSED  
48673 94 15905  
48767 1 UNUSED  
48896 33 UNUSED  
48929 94 16161  
49023 1 UNUSED  
49152 33 UNUSED  
49185 94 16417  
49279 1 UNUSED  
49408 33 UNUSED  
49441 94 16673  
49535 1 UNUSED  
49664 33 UNUSED  
49697 94 16929  
49791 1 UNUSED  
49920 33 UNUSED  
49953 94 17185  
50047 1 UNUSED  
50176 33 UNUSED  
50209 94 17441  
50303 1 UNUSED  
50432 33 UNUSED  
50465 94 17697  
50559 1 UNUSED  
50688 33 UNUSED  
50721 94 17953  
50815 1 UNUSED  
50944 33 UNUSED  
50977 94 18209  
51071 1 UNUSED  
51200 33 UNUSED  
51233 94 18465  
51327 1 UNUSED  
51456 33 UNUSED  
51489 94 18721  
51583 1 UNUSED  
51712 33 UNUSED  
51745 94 18977  
51839 1 UNUSED  
51968 33 UNUSED

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52001 94 19233  
52095 1 UNUSED  
52224 33 UNUSED  
52257 94 19489  
52351 1 UNUSED  
52480 33 UNUSED  
52513 94 19745  
52607 1 UNUSED  
52736 33 UNUSED  
52769 94 20001  
52863 1 UNUSED  
52992 33 UNUSED  
53025 94 20257  
53119 1 UNUSED  
53248 33 UNUSED  
53281 94 20513  
53375 1 UNUSED  
53504 33 UNUSED  
53537 94 20769  
53631 1 UNUSED  
53760 33 UNUSED  
53793 94 21025  
53887 1 UNUSED  
54016 33 UNUSED  
54049 94 21281  
54143 1 UNUSED  
54272 33 UNUSED  
54305 94 21537  
54399 1 UNUSED  
54528 33 UNUSED  
54561 94 21793  
54655 1 UNUSED  
54784 33 UNUSED  
54817 94 22049  
54911 1 UNUSED  
55040 33 UNUSED  
55073 94 22305  
55167 1 UNUSED  
55296 33 UNUSED  
55329 94 22561  
55423 1 UNUSED  
55552 33 UNUSED  
55585 94 22817  
55679 1 UNUSED  
55808 33 UNUSED  
55841 94 23073  
55935 1 UNUSED  
56064 33 UNUSED  
56097 94 23329  
56191 1 UNUSED  
56320 33 UNUSED  
56353 94 23585  
56447 1 UNUSED  
56576 33 UNUSED  
56609 94 23841  
56703 1 UNUSED  
56832 33 UNUSED

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56865 94 24097  
56959 1 UNUSED  
57088 33 UNUSED  
57121 94 24353  
57215 1 UNUSED  
57344 33 UNUSED  
57377 94 24609  
57471 1 UNUSED  
57600 33 UNUSED  
57633 94 24865  
57727 1 UNUSED  
57856 33 UNUSED  
57889 94 25121  
57983 1 UNUSED  
58112 33 UNUSED  
58145 94 25377  
58239 1 UNUSED  
58368 33 UNUSED  
58401 94 25633  
58495 1 UNUSED  
58624 33 UNUSED  
58657 94 25889  
58751 1 UNUSED  
58880 33 UNUSED  
58913 94 26145  
59007 1 UNUSED  
59136 33 UNUSED  
59169 94 26401  
59263 1 UNUSED  
59392 33 UNUSED  
59425 94 26657  
59519 1 UNUSED  
59648 33 UNUSED  
59681 94 26913  
59775 1 UNUSED  
59904 33 UNUSED  
59937 94 27169  
60031 1 UNUSED  
60160 33 UNUSED  
60193 94 27425  
60287 1 UNUSED  
60416 33 UNUSED  
60449 94 27681  
60543 1 UNUSED  
60672 33 UNUSED  
60705 94 27937  
60799 1 UNUSED  
60928 33 UNUSED  
60961 94 28193  
61055 1 UNUSED  
61184 33 UNUSED  
61217 94 28449  
61311 1 UNUSED  
61440 33 UNUSED  
61473 94 28705  
61567 1 UNUSED  
61696 33 UNUSED

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61729 94 28961  
61823 1 UNUSED  
61952 33 UNUSED  
61985 94 29217  
62079 1 UNUSED  
62208 33 UNUSED  
62241 94 29473  
62335 1 UNUSED  
62464 33 UNUSED  
62497 94 29729  
62591 1 UNUSED  
62720 33 UNUSED  
62753 94 29985  
62847 1 UNUSED  
62976 33 UNUSED  
63009 94 30241  
63103 1 UNUSED  
63232 33 UNUSED  
63265 94 30497  
63359 1 UNUSED  
63488 33 UNUSED  
63521 94 30753  
63615 1 UNUSED  
63744 33 UNUSED  
63777 94 31009  
63871 1 UNUSED  
64000 33 UNUSED  
64033 94 31265  
64127 1 UNUSED  
64256 33 UNUSED  
64289 94 31521  
64383 1 UNUSED  
64512 33 UNUSED  
64545 94 31777  
64639 1 UNUSED  
64768 33 UNUSED  
64801 94 32033  
64895 1 UNUSED  
65024 33 UNUSED  
65057 94 32289  
65151 1 UNUSED

CAPACITY PUBLIC "ISO 8879:1986//CAPACITY Reference//EN"  
SCOPE DOCUMENT  
SYNTAX  
SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17  
18 19 20 21 22 23 24 25 26 27 28 29 30 31 127 255  
BASESET "ISO 646-1983//CHARSET International Reference Version  
(IRV)//ESC 2/5 4/0"  
DESCSET 0 128 0  
FUNCTION RE 13  
RS 10  
SPACE 32  
TAB SEPCHAR 9  
NAMING LCNMSTRT ""  
UCNMSTRT ""  
LCNMCHAR "-."

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	UCNMCHAR	" - . "					
	NAMECASE	GENERAL	YES				
		ENTITY	NO				
DELIM	GENERAL	SGMLREF					
	SHORTREF	SGMLREF					
NAMES	SGMLREF						
QUANTITY	SGMLREF						
	ATTSPLLEN	65536					
	LITLEN	65536					
	NAMELEN	32					
	PILEN	65536					
	TAGLVL	100					
	TAGLEN	65536					
	GRPGTCNT	150					
	GRPCNT	64					
FEATURES							
MINIMIZE	DATATAG	NO	OMITTAG	NO	RANK	NO	SHORTTAG
YES							
LINK	SIMPLE	NO	IMPLICIT	NO	EXPLICIT	NO	
OTHER	CONCUR	NO	SUBDOC	NO	FORMAL	YES	
APPINFO	NONE>						

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**ichiesr-utf8.dcl** – This SGML declaration supports the ISO 10646 (UNICODE) UTF-8 character set. This character set supports almost all of the worlds currently written languages.

```
<!SGML "ISO 8879:1986 (WWW)"  
--  
    SGML Declaration for ICH SGML Applications using Unicode.  
    This Declaration is a virtual copy of the SGML Declaration  
    for HyperText Markup Language version 4.0 as modified by  
    James Clark to work with SP.  
  
    With support for the first 17 planes of ISO 10646 and  
    increased limits for tag and literal lengths etc.  
  
    Modified by jjc to work around SP's 16-bit character limit.  
    Modified by jjc to support hex character references.  
--  
  
CHARSET  
    BASESET "ISO Registration Number 177//CHARSET  
              ISO/IEC 10646-1:1993 UCS-4 with  
              implementation level 3//ESC 2/5 2/15 4/6"  
    DESCSET 0      9      UNUSED  
            9      2      9  
            11     2      UNUSED  
            13     1      13  
            14     18     UNUSED  
            32     95     32  
            127    1      UNUSED  
            128    32     UNUSED  
-- jjc: changed the rest of the DESCSET.  
Note that surrogates are not declared UNUSED;  
this allows non-BMP characters to be parsed. --  
            160    65376   160  
-- 160    55136   160  
      55296   2048   UNUSED  
      57344   1056768 57344 --  
  
CAPACITY  
    SGMLREF  
    TOTALCAP      150000  
    GRPCAP        150000  
    ENTCAP        150000  
  
SCOPE DOCUMENT  
SYNTAX  
    SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16  
          17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127  
    BASESET "ISO 646IRV:1991//CHARSET  
              International Reference Version  
              (IRV)//ESC 2/8 4/2"  
    DESCSET 0 128 0  
  
FUNCTION  
    RE      13  
    RS      10  
    SPACE   32  
    TAB SEPCHAR 9
```

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```
NAMING      LCNMSTRT  ""
UCNMSTRT   ""
LCNMCHAR   ".-_:"
UCNMCHAR   ".-_:"
NAMECASE   GENERAL YES
                ENTITY NO
DELIM       GENERAL SGMLREF
                HCRO "&#38;#X" -- added by jjc --
                SHORTREF SGMLREF
NAMES       SGMLREF
QUANTITY    SGMLREF
                ATTCNT   60      -- increased --
                ATTSPLEN 65536   -- These are the largest values --
                LITLEN    65536   -- permitted in the declaration --
                NAMELEN   32      -- Avoid fixed limits in actual --
                PILEN    65536   -- implementations of HTML UA's --
                TAGLVL    100
                TAGLEN    65536
                GRPGTCNT 150
                GRPCNT   64

FEATURES
MINIMIZE
DATATAG    NO
OMITTAG   NO
RANK       NO
SHORTTAG  YES
LINK
SIMPLE    NO
IMPLICIT  NO
EXPLICIT  NO
OTHER
CONCUR    NO
SUBDOC    NO
FORMAL    YES
APPINFO   NONE
>
```

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**ichiesr-mult.dcl** – Running in direct contradiction to what has been said up to this point, this SGML declaration will support all of the currently defined ICHICSR languages, and it doesn't require the use of UNICODE. It is however a "hack" that relies on a fortuitous characteristic of the languages currently being used within the ICHICSR SGML application.

This hack works because the character set documented within an SGML declaration is for the benefit of both the SGML parser, and the programmer who implements the SGML application. The programmer needs detailed knowledge of **all** the characters being used to correctly code an application. The parser only really needs to about **some** of the characters. In particular it needs to know which characters signify an SGML event. For instance that the "<" character starts an SGML open tag , and the "</" character sequence starts an SGML close tag. All told, the parser needs to know very little. Because of the particular combination of character sets being used within the ICHICSR application, an SGML declaration can be defined that tells the parser just what it needs to know and still work across all of the different character sets. The catch is that this SGML declaration doesn't tell the programmer all that she or he needs to know to correctly code the rest of the application. If this declaration is used, the programmer will have to get this detailed information from another source.

```
<! SGML  "ISO 8879:1986"
--
      SGML Declaration for ICHICSR SGML Applications that will
      allow an SGML parser to parse SJIS, and ISO Latin 1-9 without an error.

      Note: This is not strictly speaking a correct SGML declaration, as
      it does not correctly document the character set being used.
      Instead, it simply ignores all characters except for the ones that are
      important to the SGML parser. These characters are expected to be found
      at the standard ASCII code points.

      With support for increased limits for tag and literal lengths etc.
--

CHARSET
      BASESET  "ISO 646:1983//CHARSET
                  International Reference Version
                  (IRV)//ESC 2/5 4/0"
      DESCSET   0    9    UNUSED
                9    2    9
                11   2    UNUSED
                13   1    13
                14   18   UNUSED
                32   95   32
                127  1    UNUSED
      BASESET  "ISO Registration Number 100//CHARSET
                  ECMA-94 Right Part of
                  Latin Alphabet Nr. 1//ESC 2/13 4/1"
      DESCSET   128  127  128
                255  1    UNUSED

CAPACITY  SGMLREF
      TOTALCAP      200000
      GRPCAP        150000
      ENTCAP        150000

SCOPE     DOCUMENT
SYNTAX
      SHUNCHAR CONTROLS 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
```

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17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 127  
BASESET "ISO 646:1983//CHARSET  
International Reference Version  
(IRV)//ESC 2/5 4/0"  
DESCSET 0 128 0

FUNCTION  
RE 13  
RS 10  
SPACE 32  
TAB SEPCHAR 9

NAMING LCNMSTRT ""  
UCNMSTRT ""  
LCNMCHAR ". -"  
UCNMCHAR ". -"  
NAMECASE GENERAL YES  
ENTITY NO

DELIM GENERAL SGMLREF  
SHORTREF SGMLREF

NAMES SGMLREF

QUANTITY SGMLREF  
ATTSPLEN 65536  
LITLEN 65536  
NAMELEN 32  
PILEN 65536  
TAGLVL 100  
TAGLEN 65536  
GRPGTCNT 150  
GRPCNT 64

FEATURES  
MINIMIZE  
DATATAG NO  
OMITTAG NO  
RANK NO  
SHORTTAG YES

LINK  
SIMPLE NO  
IMPLICIT NO  
EXPLICIT NO

OTHER  
CONCUR NO  
SUBDOC NO  
FORMAL YES

APPINFO NONE

>

#### A.4 ICH M2 Numeric Codes for Unit List (E2B Attachment 1)

Please use the ICH M2 numeric codes to populate fields that require the E2B unit list (Attachment 1).

Unit List	ICH-M2 Numeric Codes
<b>Mass</b>	
kg kilogram(s)	001
G gram(s)	002
Mg milligram(s)	003
µg microgram(s)	004
ng nanogram(s)	005
pg picogram(s)	006
mg/kg milligram(s)/kilogram	007
µg/kg microgram(s)/kilogram	008
mg/m <sup>2</sup> milligram(s)/sq. meter	009
µg/m <sup>2</sup> microgram(s)/ sq. meter	010
<b>Volume</b>	
l litre(s)	011
ml millilitre(s)	012
µl microlitre(s)	013
<b>Radioactivity</b>	
Bq becquerel(s)	014
GBq gigabecquerel(s)	015
MBq megabecquerel(s)	016
Kbq kilobecquerel(s)	017
Ci curie(s)	018
MCi millicurie(s)	019
µCi microcurie(s)	020
NCi nanocurie(s)	021
<b>Other</b>	
Mol mole(s)	022
Mmol millimole(s)	023
µmol micromole(s)	024
Iu international unit(s)	025
Kiu iu(1000s)	026
Miu iu(1,000,000s)	027
iu/kg iu/kilogram	028
Meq milliequivalent(s)	029

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%	percent	030
Gtt	drop(s)	031
DF	dosage form	032
<b>Definition of Interval List</b>		<b>Proposed ICH-M2 Codes</b>
Seconds		807
Minutes		806
Hours		805
Days		804
Weeks		803
Months		802
Years		801
Trimester		810
Cyclical		811
As Necessary		812
Total		813

## A.5 Routes of Administration (E2B Attachment 2)

Please use the ICH M2 numeric codes to populate fields that require the E2B routes of administration (Attachment 2).

Description	ICH M2 Numeric Codes
Auricular (otic)	001
Buccal	002
Cutaneous	003
Dental	004
Endocervical	005
Endosinusial	006
Endotracheal	007
Epidural	008
Extra-amniotic	009
Hemodialysis	010
Intra corpus cavernosum	011
Intra-amniotic	012
Intra-arterial	013
Intra-articular	014
Intra-uterine	015
Intracardiac	016
Intracavernous	017
Intracerebral	018
Intracervical	019
Intracisternal	020
Intracorneal	021
Intracoronary	022
Intradermal	023
Intradiscal (intraspinal)	024
Intrahepatic	025
Intralesional	026
Intralymphatic	027
Intramedullar (bone marrow)	028
Intrameningeal	029
Intramuscular	030
Intraocular	031
Intrapericardial	032
Intrapерitoneal	033
Intrapleural	034
Intrasyновial	035
Intratumor	036
Intrathecal	037
Intrathoracic	038
Intratracheal	039
Intravenous bolus	040
Intravenous drip	041

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Intravenous (not otherwise specified)	042
Intravesical	043
Iontophoresis	044
Nasal	045
Occlusive dressing technique	046
Ophthalmic	047
Oral	048
Oropharyngeal	049
Other	050
PARENTERAL	051
Periarticular	052
Perineural	053
Rectal	054
Respiratory (inhalation)	055
Retrobulbar	056
Sunconjunctival	057
Subcutaneous	058
Subdermal	059
Sublingual	060
Topical	061
Transdermal	062
Transmammary	063
Transplacental	064
Unknown	065
Urethral	066
Vaginal	067

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## A.6 ICH ICSR Acknowledgment Message

The ICSR Acknowledgment Message is being provided to help Industry and Regulators verify the usability and compliance of the transmitted data as per ICH recommendations. The ICSR Acknowledgment Message is comprised of two sections, each occurring once; the ICSR message header section and the acknowledgment section. The acknowledgment section is comprised of two portions, a message acknowledgment portion which occurs once, and a report acknowledgment portion which can occur one time, many times, or not at all. The acknowledgment sections can be used to communicate to the sender the results of the validation of the transmitted data set. Listed below are the details of the specification:

Data Element	Title	Description	DTD Descriptor	Field Length	Field Value	Required
M.1	ICSR Message Header	Header/Entity	ichicsrmessaghea der			
M.1.1	Message Type	Type of Information Being Transmitted	messagetype	16 AN	ichicsrack	Yes
M.1.2	Message Format Version	Version Number of Message Format	messageformatvers ion	3AN		Yes
M.1.3	Message Format Release	Release number of the Message Format	messageformatrele ase	3AN		Yes
M.1.4	Message Number	Message Number	messagenumb	100AN		Yes
M.1.5	Message Sender Identifier	Message Sender Identifier	messagesenderiden tifier	60AN		Yes
M.1.6	Message Receiver Identifier	Message Receiver Identifier	messagereceiverid entifier	60AN		Yes
M.1.7a	Message Date	Message Date Format	messagedateformat	3N	204 – Format CCYYMM DDHHMM SS	Yes
M.1.7b	Message Date		messagedate	14N	CCYYMM DDHHMM SS	Yes
A.1	Message Acknowledgment	Header/Entity	messageacknowled gment			
A.1.1	ICSR Message Number	Message Number	icsrmessagenumb	100AN		Yes
A.1.2	Local Message Number	Local Message Number	localmessagenumb	100AN	Locally Assigned	
A.1.3	ICSR Message Sender ID	Message Sender Identifier	icsrmessagesenderi dentifier	60AN		Yes
A.1.4	ICSR Message Receiver ID	Message Receiver Identifier	icsrmessagereceive ridentifier	60AN		Yes
A.1.5a	ICSR Message Date	Message Date Format	icsrmessagedatefor mat	3N	204 – Format CCYYMM DDHHMM SS	Yes
A.1.5b	ICSR Message Date		icsrmessagedate	14N	CCYYMM DDHHMM SS	Yes

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A.1.6	Transmission Acknowledgment Code	Response from Agency on Transmission	transmissionacknowledgmentcode	2N	01= All Reports loaded into database 02 = ICSR Error, not all reports loaded into the database, check section B 03= SGML parsing error, no data extracted	Yes
A.1.7	Parsing Error Message	Description of the SGML Parsing Error Encountered	parsingerrormessage	250 AN		
B.1.	Report Acknowledgment	Header/Entity	reportacknowledgment			
B.1.1	Safety Report ID	Safety Report Identifier	safetyreportid	100AN		
B.1.2	Safety Report Version Number		safetyreportversion	2AN		
B.1.3	Local Report Number		localreportnumber	100AN		
B.1.4	National regulatory authority's case report number (E2B- A.1.10.1)		authoritynumber	100AN		
B.1.5	Company's case report number (E2B- A.1.10.2)		companynumber	100AN		
B.1.6	Other sender's case report number (E2B- A.1.10.3)		othernumber	100AN		
B.1.7a	Date of receipt of the most recent information (E2B- A.1.7)	Receipt Date Format	receiptdateformat	3N	102 – Format CCYYMM DD	
B.1.7b	Date of receipt of the most recent information (E2B- A.1.7)		receiptdate	8N	CCYYMM DD	
B.1.8	Acknowledgment Code for a Report	Report Level Acknowledgment (If there is an error code, re-send only the specified report.)	reportacknowledgmentcode	2N	01=Report Loaded Successfully 02=Report Not Loaded	Yes
B.1.9	Error Message or Comment	Description of the Specific Error or Errors Encountered	errormessagecomment	250AN		

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Note: The double line border depicts a repeatable block

## **Element Descriptions for Acknowledgment of ICSRs**

### **M.1 ICSR Message Header**

This is the standard ICH M2 message header, similar to the message header in the ICH ICSR DTD. This section specifies the message type, such as ICSR Acknowledgments, version, and release number of the DTD. This message header section assumes the establishment of an EDI trading partnership agreement that will help drive the designation of the message identification number, sender ID, receiver ID, message date, and the acknowledgment for the submission of the SGML file containing multiple ICSRs.

#### **M.1.1 Message type**

The message type contains information on the type of information being transmitted. It is specified in ESTRI recommendation 5.3. When creating an ICSR Acknowledgment SGML message, the value of this field should be “ichicsrack”.

#### **M.1.2 Message Format Version**

The message format version contains the version number of the DTD and it is specified in ESTRI recommendation 5.3. The value of the version number can be obtained from the documentation section of the ICSR Acknowledgment Message DTD.

#### **M.1.3 Message Format Release**

The message format release contains the release number of the message format version number of the DTD and it is specified in ESTRI recommendation 5.3. The value of the release number can be obtained from the documentation section of the ICSR Acknowledgment Message DTD.

#### **M.1.4 Message Number, sender defined message number (unique to the sender)**

The message number is a unique tracking number assigned to a specific acknowledgment message file by the sender of the acknowledgment. This message number is unique to the sender.

#### **M.1.5 Message Sender Identifier**

This field identifies the sender of the acknowledgment, e.g. receiver of the ICH ICSR message, ICSR Attribute List A.3.2.2a.

#### **M.1.6 Message Receiver Identifier**

This field identifies the receiver of the acknowledgment, e.g. sender of the ICH ICSR message, ICSR Attribute List A.3.1.2.

#### **M.1.7a and b Message Date and Format**

The message date is the date on which the acknowledgment message was initiated.

### **A.1 Message Acknowledgment**

This is a section header that specifies the ICH ICSR message that is being acknowledged. This section also assumes the establishment of an EDI trading partnership agreement that will help drive the designation of the message identification number, local message number, sender ID, receiver ID, message date, and the acknowledgment for the submission of the SGML file containing multiple ICSRs.

#### **A.1.1 ICSR Message Number, Sender defined message number (unique to the sender)**

The ICSR message number is a unique tracking number assigned to a specific ICH ICSR message file by the sender. This ICSR message number is unique to the sender of the ICH ICSR message.

**A.1.2 Local Message Number**

The local message number is a value assigned to the ICH ICSR message by the receiving organization. The length, data type, and value are determined by the receiving organization.

**A.1.3 ICSR Message Sender Identifier**

This field identifies the sender of the ICSR reports, e.g. ICSR Attribute List A.3.1.2, sender of case safety report forms.

**A.1.4 ICSR Message Receiver Identifier**

This field identifies the receiver of the ICSR reports, e.g. ICSR Attribute List A.3.2.2a, receiver of case safety report forms.

**A.1.5a and b ICSR Message Date and Format**

The ICSR message date is the date on which the ICH ICSR message was initiated.

**A.1.6 Transmission Acknowledgment Code**

The transmission acknowledgment field is a 2AN field that will inform the sender of the ICH ICSR message to either re-send the complete transmission or await acknowledgment on individual reports.

Values:

01 = All Reports loaded into database

02 = ICSR Error, not all reports loaded into the database, check section B

03 = SGML parsing error, no data extracted

**A.1.7 Parsing Error Message**

The Parsing Error Message field is a 250 character field that can be used to briefly describe the types of SGML errors detected while parsing the file. This field is used when the value of A.1.6 is 03.

**B.1. Report Acknowledgment**

This is a section header for acknowledging each report included in the ICH ICSR message file. This section specifies the required elements to acknowledge the data format, data length, and data type, to ensure the information is loadable into the receiver's database. This section will be a repeatable section for each report that will be acknowledged. This section will be included in the acknowledgment message if the value for A.1.6 above is "02". In other words, there can be 0 to many occurrences of this section.

**B.1.1 Safety Report ID**

The safety report identifier is the number assigned by the sender to identify each ICSR.

**B.1.2 Safety Report Version Number**

The safety report version is a number assigned by the sender of the ICSR to differentiate the different versions of an ICSR.

**B.1.3 Local Report Number**

The local report number is a value assigned to each ICSR by the receiving organization of the ICH ICSR message.

**B.1.4 National Regulatory Authority's Case Report Number (E2B: A.1.10.1).**

B.1.4 is a unique identifier that is equivalent to the national regulatory authority's case report number. It will be the same value assigned to the E2B field A.1.10.1.

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**B.1.5 Company's Case Report Number (E2B: A.1.10.2)**

B.1.5 is a company unique identifier assigned by a company and is the same as the value assigned to E2B field A.1.10.2. As the E2B Step 4 document specifies, companies should ensure a single international number to facilitate the unique identification of a report that may have been sent to many places and subject to multiple re-transmissions.

**B.1.6 Other Sender's Case Report Number (E2B: A.1.10.3)**

B.1.6 will be used by senders who are not representing either a pharmaceutical company or a national regulatory authority. It is the same as the value assigned to the E2B field A.1.10.3.

**B.1.7 a and b Date of Receipt of the Most Recent Information (E2B: A.1.7)**

This field must be used to record the date of the most recent information of the case. It is the same as the value assigned to the E2B field A.1.7.

**B.1.8 Acknowledgment Code for a Report**

This field will be used to indicate if a report was successfully loaded into the application data base or if it failed the loading process. If there is an error, the application may indicate the nature of the error in the text field B.1.9. The field B.1.8 is 2AN and will contain one of following values:

01 = Report Loaded Successfully

02 = Report Not Loaded

**B.1.9 Error Message or Comment**

This field is a 250 character field that can be used to briefly describe the error message and the relevant field to help the sender of the ICSR correct the problem. This field is not intended to contain a complete list of errors found with a report. The extent of the error reporting is application dependent. As a minimum the application should describe the first error encountered when trying to load a report into the database.

## A.7 ICH ICSR Acknowledgment DTD

```
<!DOCTYPE ichicsrack [
<!-- PUBLIC "-//ICHM2//DTD ICH ICSR Acknowledgment Vers. 1.0//EN" "ich-icsrack-v1.0.dtd" --&gt;
&lt;!--
Individual Case Safety Report Acknowledgment Document Type Definition</pre>
```

The DTD issued by the ICH M2 group and is public domain in nature.

No one can claim copyright on this DTD.  
No commercial distribution is allowed.

The ICH is not responsible for any damage or financial loss resulting from use of this DTD. This version is tentative in nature and changes are expected. This DTD is subject to the ICH M2 change control procedures.

Version 1.0, Release 1.0, Date to be decided

-->

<!-- TECHNICAL NOTE

### ICH ICSR SGML Declaration

To correctly parse an ICH ICSR SGML message requires the selection of the correct SGML declaration, along with this DTD, and the ICH ICSR SGML instance. This technical note provides guidance on which of several SGML declarations included with the ICH ICSR application to select based on the language and character set used within the ICH ICSR SGML instance. The method by which an SGML parser is told to use a specific declaration is parser specific. The three most common methods are:

1. Tell the parser via the command line which declaration to use.
2. Tell the parser via a specific environment variable which declaration to use.
3. If the parser supports SGML Open catalogs, within the catalog file is a command that can tell the parser which declaration to use. SGML catalog files are an industry standard way to tell a parser how to find all of the pieces (declaration, DTD, SGML document instance) needed to successfully parse.

To cover all of the languages necessary to support the ICH ICSR application, ISO 10646 (UNICODE) would have to be used. If this were the case, then only one SGML declaration would be needed to support all ICH ICSR languages. Because UNICODE support is not available in all popular computer application programs, the ICH M2 EWG has recommended that a variety of character sets be used at this time, instead of a single UNICODE character encoding. For each of these different character encodings a different SGML declaration needs to be generated and used.

Five SGML declarations are included with the ICH ICSR distribution. They are described briefly below.

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ich-icsr-latin1.dcl - This SGML declaration supports the ISO 8859-1 (Latin 1) character set. This character set supports English, and most Western European languages.

ich-icsr-latin7.dcl - This SGML declaration supports the ISO 8859-7 (Latin 7) character set. This character set supports Greek.

ich-icsr-sjis.dcl - This SGML declaration supports the Shift JIS character set for encoding Japanese.

ich-icsr-utf8.dcl - This SGML declaration supports the ISO 10646 (UNICODE) UTF-8 character set. This character set supports almost all of the worlds currently written languages.

ich-icsr-mult.dcl - This SGML declaration will support all of the currently defined ICHICSR languages, and it doesn't require the use of UNICODE. It is however a "hack" that relies on a fortuitous characteristic of the languages currently being used within the ICH ICSR SGML application.

This hack works because the character set documented within an SGML declaration is for the benefit of both the SGML parser, and the programmer who implements the SGML application. The programmer needs detailed knowledge of all the characters being used to correctly code an application. The parser only really needs to about some of the characters. In particular it needs to know which characters signify an SGML event. For instance that the "<" character starts an SGML open tag, and the "</" character sequence starts an SGML close tag. All told, the parser needs to know very little. Because of the particular combination of character sets being used within the ICH ICSR application, an SGML declaration can be defined that tells the parser just what it needs to know and still work across all of the different character sets. The catch is that this SGML declaration doesn't tell the programmer all that she or he needs to know to correctly code the rest of the application. If this declaration is used, the programmer will have to get this detailed information from another source.

```
-->

<!-- ====== -->
<!-- Entities -->
<!-- ====== -->

<!-- Use the lang attribute to indicate the language of an -->
-- elements content via an ISO 639 language Code. -->

<!ENTITY % lang.att "lang CDATA #IMPLIED">

<!-- Standard Character Entities to escape SGML special characters. --
-- When "<", ">", and "&" occur in text, they should be replaced --
-- by "&lt;", "&gt;", and "&amp;" respectfully. -->

<!-- Less Than "<" -->
<!ENTITY lt "&#38;#60;">

<!-- Greater Than ">" -->
<!ENTITY gt "&#62;">
```

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```
<!-- Ampersand "&" -->
<!ENTITY amp  "&#38;#38;">

<!-- ===== -->
<!-- Elements and Attributes                               -->
<!-- ===== -->

<!ELEMENT ichicsrack      --
          (ichicsrmessageheader      ,
           acknowledgment)>
<!ATTLIST ichicsrack
         lang      CDATA #REQUIRED
>

<!-- M.1 ICH ICSR Message Header Information -->

<!ELEMENT ichicsrmessageheader      --
          (messagetype      ,
           messageformatversion      ,
           messageformatrelease      ,
           messagenumb      ,
           messagesenderidentifier      ,
           messagereceiveridentifier      ,
           messagedateformat      ,
           messagedate)>
<!ATTLIST ichicsrmessageheader
         %lang.att;
>

<!-- M.1.1 Message Type -->
<!ELEMENT messagetype      -- (#PCDATA) >
<!ATTLIST messagetype
         %lang.att;
>

<!-- M.1.2 Message Format Version -->
<!ELEMENT messageformatversion      -- (#PCDATA) >
<!ATTLIST messageformatversion
         %lang.att;
>

<!-- M.1.3 Message Format Release -->
<!ELEMENT messageformatrelease      -- (#PCDATA) >
<!ATTLIST messageformatrelease
         %lang.att;
>

<!-- M.1.4 Message Number -->
<!ELEMENT messagenumb      -- (#PCDATA) >
<!ATTLIST messagenumb
         %lang.att;
>

<!-- M.1.5 Message Sender Identifier -->
<!ELEMENT messagesenderidentifier -- (#PCDATA) >
<!ATTLIST messagesenderidentifier
```

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```
%lang.att;
>

<!-- M.1.6 Message Receiver Identifier -->
<!ELEMENT messagereceiveridentifier - - (#PCDATA) >
<!ATTLIST messagereceiveridentifier
      %lang.att;
>

<!-- M.1.7a Message Date Format -->
<!ELEMENT messagedateformat    - -   (#PCDATA)>
<!ATTLIST messagedateformat
      %lang.att;
>

<!-- M.1.7b Message Date -->
<!ELEMENT messagedate      - -   (#PCDATA) >
<!ATTLIST messagedate
      %lang.att;
>

<!-- A.1 ICSR Acknowledgment Message-->
<!ELEMENT acknowledgment      - -
      (messageacknowledgment
       reportacknowledgment*)>
<!ATTLIST acknowledgment
      %lang.att;
>

<!-- A.1 Message Acknowledgment -->
<!ELEMENT messageacknowledgment      - -
      (icsrmessagenumb
       localmessagenumb?
       icssmessagesenderidentifier
       icssmessagereceiveidentifier
       icssmessagedateformat
       icssmessagedate
       transmissionacknowledgmentcode
       parsingerrormessage?)>
<!ATTLIST messageacknowledgment
      %lang.att;
>

<!-- A.1.1 ICSR Message Number -->
<!ELEMENT icssmessagenumb      - -   (#PCDATA)>
<!ATTLIST icssmessagenumb
      %lang.att;
>

<!-- A.1.2 Local Message Number -->
<!ELEMENT localmessagenumb    - -   (#PCDATA)>
<!ATTLIST localmessagenumb
      %lang.att;
>

<!-- A.1.3 ICSR Message Sender Identifier -->
```

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```
<!ELEMENT icsrmessagesenderidentifier --      (#PCDATA)>
<!ATTLIST icsrmessagesenderidentifier
          %lang.att;
>

<!-- A.1.4 ICSR Message Receiver Identifier -->
<!ELEMENT icsrmessagereceiveridentifier --      (#PCDATA)>
<!ATTLIST icsrmessagereceiveridentifier
          %lang.att;
>

<!-- A.1.5a ICSR Message Date Format -->
<!ELEMENT icsrmessagedateformat  --  (#PCDATA)>
<!ATTLIST icsrmessagedateformat
          %lang.att;
>

<!-- A.1.5b ICSR Message Date -->
<!ELEMENT icsrmessagedate    --      (#PCDATA)>
<!ATTLIST icsrmessagedate
          %lang.att;
>

<!-- A.1.6 Transmission Acknowledgment -->
<!ELEMENT transmissionacknowledgmentcode --  (#PCDATA)>
<!ATTLIST transmissionacknowledgmentcode
          %lang.att;
>

<!-- A.1.7 Parsing Error Message -->
<!ELEMENT parsingerrormessage --      (#PCDATA)>
<!ATTLIST parsingerrormessage
          %lang.att;
>

<!-- B.1 Report Acknowledgment -->
<!ELEMENT reportacknowledgment      --
          (safetyreportid?
           , safetyreportversion?
           , localreportnumb?
           , authoritynumb?
           , companynumb?
           , othernumb?
           , receiptdateformat?
           , receiptdate?
           , reportacknowledgmentcode
           , errormessagecomment?)>
<!ATTLIST reportacknowledgment
          %lang.att;
>

<!-- B.1.1 Safety Report Identification -->
<!ELEMENT safetyreportid      --  (#PCDATA)>
<!ATTLIST safetyreportid
          %lang.att;
>
```

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```
<!-- B.1.2 Safety Report Version -->
<!ELEMENT safetyreportversion  - -  (#PCDATA)>
<!ATTLIST safetyreportversion
      %lang.att;
>

<!-- B.1.3 Local Report Number -->
<!ELEMENT localreportnumb    - -  (#PCDATA)>
<!ATTLIST localreportnumb
      %lang.att;
>

<!-- B.1.4 National regulatory authority's case report number (E2B - A.1.10.1)-->
<!ELEMENT authoritynumb      - -  (#PCDATA)>
<!ATTLIST authoritynumb
      %lang.att;
>

<!-- B.1.5 Company's case report number (E2B - A.1.10.2) -->
<!ELEMENT companynumb        - -  (#PCDATA)>
<!ATTLIST companynumb
      %lang.att;
>

<!-- B.1.6 Other sender's case report number (E2B - A.1.10.3) -->
<!ELEMENT othernumb         - -  (#PCDATA)>
<!ATTLIST othernumb
      %lang.att;
>

<!-- B.1.7a Receipt Date Format -->
<!ELEMENT receiptdateformat  - -  (#PCDATA)>
<!ATTLIST receiptdateformat
      %lang.att;
>

<!-- B.1.7b Date of receipt of the most recent information (E2B - A.1.7) -->
<!ELEMENT receiptdate        - -  (#PCDATA)>
<!ATTLIST receiptdate
      %lang.att;
>

<!-- B.1.8 Acknowledgment Code for a report -->
<!ELEMENT reportacknowledgmentcode  - -  (#PCDATA)>
<!ATTLIST reportacknowledgmentcode
      %lang.att;
>

<!-- B.1.9 Error Message or Comment -->
<!ELEMENT errormessagecomment   - -  (#PCDATA)>
<!ATTLIST errormessagecomment
      %lang.att;
>
]>
```

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**A.8 Sample SGML Data File for the ICH ICSR Acknowledgment DTD**

```
<ichicsrack lang="en">
  <ichicsrmessageheader>
    <messagetype>ichicsrrack</messagetype>
    <messageformatversion>1.0</messageformatversion>
    <messageformatrelease>1.0</messageformatrelease>
    <messagenumb>00000010016328</messagenumb>
    <messagesenderidentifier>FDA</messagesenderidentifier>
    <messagereceiveridentifier>pharmaceutical
company</messagereceiveridentifier>
    <messagedateformat>204</messagedateformat>
    <messagedate>19980716</messagedate>
  </ichicsrmessageheader>
  <acknowledgment>
    <messageacknowledgment>
      <icsrmessagenumb>100052365478900</icsrmessagenumb>
      <localmessagenumb></localmessagenumb>
      <icsrmessagesenderidentifier>pharmaceutical
company</icsrmessagesenderidentifier>
      <icsrmessagereceiveridentifier>FDA</icsrmessagereceiveridentifier>
      <icsrmessagedateformat>102</icsrmessagedateformat>
      <icsrmessagedate>19980715</icsrmessagedate>
      <transmissionacknowledgmentcode>02</transmissionacknowledgmentcode>
      <parsingerrormessage></parsingerrormessage>
    </messageacknowledgment>
    <reportacknowledgment>
      <safetyreportid></safetyreportid>
      <safetyreportversion></safetyreportversion>
      <localreportnumb>US-FDA-authority report number 10052410</localreportnumb>
      <authoritynumb></authoritynumb>
      <companynumb>US-pharmaceutical company-Report1</companynumb>
      <othernumb></othernumb>
      <receiptdateformat>102</receiptdateformat>
      <receiptdate>19980701</receiptdate>
      <reportacknowledgmentcode>02</reportacknowledgmentcode>
      <errormessagecomment>there are several errors that must be corrected
before re-submitting: check field lengths and ISO codes for REACTION section
of report.</errormessagecomment>
    </reportacknowledgment>
  </acknowledgment>
</ichicsrack>
```

## A.9 Agreement on Unique Identifier

### **Proposed Resolution for the Unique Identification of the Individual Case Safety Report:**

It is necessary to uniquely identify case safety reports transmitted from companies to other companies, companies to authorities, and between authorities. M2 has referenced the E2B Step 4 document to derive an explicit technical solution for uniquely identifying reports. While the intent of the E2B document concurs with the need for unique identification, M2 has not been able to find a technical solution agreeable to the 6 parties based on the E2B specification alone. If a more specific guideline pertaining to three of the E2B elements can be accepted by the ICH Steering Committee, M2 can implement a technical solution for uniquely identifying ICSR's agreeable to all members.

Therefore, the M2 EWG requests the following amendment be made to the E2B Step 4 Document:

#### **A.1.10.1 National regulatory authority's case report number**

#### **A.1.10.2 Company's case report number**

#### **A.1.10.3 Other sender's case report number**

##### User Guidance:

A.1.10.1 and A.1.10.2 are the identifiers given by a national regulatory authority and by a company, respectively. A.1.10.3 would be used by senders who are not representing either a pharmaceutical company or a national regulatory authority. The contents of A.1.10.1, A.1.10.2, or A.1.10.3 should be populated only once, and all of these three items should remain unchanged for any transmissions subsequent to the original transmission. That is to say, these fields must only be populated once by the originator of the first transmission. Companies should ensure a single international report number (A.1.10.2) to facilitate the unique identification of a report that may have been sent to many places and subject to multiple retransmissions. The contents of the fields A.1.10.1 and/or A.1.10.2 and/or A.1.10.3 should first list A.1.1 - Identification of the country of primary source and secondly list A.3.1.2 - Sender Identifier, Sender Organization, and lastly, the company international case report number, delimited by hyphens.

For example, a report transmitted by a US company to a regulatory authority would populate A.1.10.2 with "US-*Company Name-12345*", where "*12345*" is the company's unique case report number. In the event that the regulatory authority transmitted this ICSR to another regulatory authority, A.1.10.2 would remain the same. The regulatory authority would not populate A.1.10.1.

If the situation occurs where multiple reports are received about the same case, such as a report from a physician and a report from another company, the information may be merged. One number will be maintained as the case number in its original field and the second number will be listed as a suspected duplicate.

If this definition can be adopted, then a technical solution can be agreed upon by M2. Additionally, this solution would preclude the need for any previously discussed proposals for unique identification.

## B.0 GLOSSARY

**DCL** SGML Declaration File

**DTD** Document Type Definition

**EWG** Expert Working Group

**ICH** International Conference on Harmonisation

**ICH\_ICSR.DTD** Individual Case Safety Report Document Type Definition

**ICSR** Individual Case Safety Report

**Rec. 5.2** ICH M2 Recommendation 5.2: SGML DTD Electronic Format for the Exchange of Individual Case Safety reports (E2B Message)

**Rec. 5.3** ICH M2 Recommendation 5.3: EDI Header Specification for the E2B Message

**SGML** Standard Generalized Mark-up Language